ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼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

Fluad Tetra, suspension for injection in pre-filled syringe
Influenza vaccine (surface antigen, inactivated, adjuvanted)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Influenza virus surface antigens (haemagglutinin and neuraminidase), inactivated, of the following strains*:

	Per 0.5 ml dose
A/xxxxx (H1N1) - like strain (*reassortant used*)	15 micrograms HA**
A/xxxxx (H3N2) - like strain (*reassortant used*)	15 micrograms HA**
B/xxxxx – like strain (*reassortant used*)	15 micrograms HA**
B/xxxxx – like strain (*reassortant used*)	15 micrograms HA**

*propagated in fertilised hens' eggs from healthy chicken flocks and adjuvanted with MF59C.1
**haemagglutinin

Adjuvant MF59C.1 containing per 0.5 ml dose: squalene (9.75 mg), polysorbate 80 (1.175 mg), sorbitan trioleate (1.175 mg), sodium citrate (0.66 mg) and citric acid (0.04 mg).

This vaccine complies with the WHO recommendations (Northern Hemisphere) and EU recommendation for the xxxx/xxxx season.

Fluad Tetra may contain traces of eggs such as ovalbumin or chicken proteins, kanamycin and neomycin sulphate, formaldehyde, hydrocortisone, cetyltrimethylammonium bromide (CTAB) which are used during the manufacturing process (see section 4.3).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection in pre-filled syringe (injection).
Milky-white suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Prophylaxis of influenza in the elderly (65 years of age and older).

Fluad Tetra should be used in accordance with official recommendations.

4.2 Posology and method of administration

Posology

One 0.5 ml dose.

Paediatric population

The safety and efficacy of Fluad Tetra in children from birth to less than 18 years has not been established. Currently available safety and immunogenicity data in children from 6 months to less than 6 years of age are described in sections 4.8 and 5.1 but no recommendation on posology can be made.

Method of administration

For intramuscular injection only.

The preferred injection site is the deltoid muscle of the upper arm.

The vaccine must not be injected intravenously, subcutaneously or intradermally and must not be mixed with other vaccines in the same syringe.

For instructions for preparation of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substances, to any of the components of the adjuvant, to any of the excipients listed in section 6.1, or to possible trace residues such as ovalbumin, kanamycin and neomycin sulphate, formaldehyde, cetyltrimethylammonium bromide (CTAB) and hydrocortisone.

A severe allergic reaction (e.g. anaphylaxis) to previous influenza vaccination.

4.4 Special warnings and precautions for use

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine.

Vaccination should be postponed in patients with acute febrile illness until the fever is resolved.

As with all injectable vaccines, Fluad Tetra must be administered with caution to individuals with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration.

Syncope (fainting) can occur following, or even before, any vaccination 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.

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

A protective immune response may not be elicited in all vaccine recipients.

4.5 Interaction with other medicinal products and other forms of interaction

No clinical data on concomitant administration of Fluad Tetra with other vaccines are available. If Fluad Tetra is to be used at the same time as another vaccine, it should be administered at separate injection sites and preferably on different limbs. It should be noted that the adverse reactions may be intensified by any co-administration.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
This medicine is not indicated in women of childbearing potential (see section 4.1). It is not to be used in women who are, or may be, pregnant or breast-feeding.

Pregnancy
There are no data from the use of Fluad Tetra in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of the safety profile

Elderly population
The safety of Fluad Tetra in elderly subjects 65 years of age and older was evaluated in two clinical studies (V118_20 and V118_18), in which 4269 received Fluad Tetra.

Solicited local and systemic adverse reactions were collected for 7 days after vaccination. Unsolicited adverse reactions were collected for 21 days after vaccination.

The most commonly reported (≥10%) adverse reactions across both studies were injection site pain (16.3% and 31.9%), fatigue (10.5% and 16.0%) and headache (10.8% and 12.0%) (for V118_18 and V118_20, respectively). Most solicited reactions were reported as mild or moderate in intensity and resolved within the first 3 days after vaccination.

Paediatric population

Fluad Tetra is not indicated for use in children, see section 4.2. Safety information in the paediatric population is presented in section 5.1.

Tabulated list of adverse reactions

Adverse reactions reported are listed according to the following frequency categories: Very common (≥1/10); Common (≥1/100 - <1/10); Uncommon (≥1/1,000 - <1/100).

Table 1: Adverse reactions reported following vaccination in elderly subjects 65 years and older in clinical trials

MedDRA System Organ class	Very common (≥1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)
Metabolism and nutrition disorders		Loss of appetite	
Nervous system disorders	Headache		
Gastrointestinal disorders		Nausea, Diarrhoea	Vomiting
Musculoskeletal and connective tissue disorders		Myalgia, Arthralgia	
General disorders and administration site conditions	Injection site pain, Fatigue	Ecchymosis*, Chills, Erythema, Induration, Influenza-like illness	Fever (≥ 38°C)

*Or Injection site bruising

Adverse reactions reported from post-marketing surveillance

There are currently no post-marketing data available for Fluad Tetra. However, the post-marketing experience with Fluad (trivalent formulation) is relevant to Fluad Tetra because both vaccines are manufactured using the same process and have overlapping compositions. The following adverse reactions were reported from post marketing surveillance with Fluad (trivalent formulation):

Blood and lymphatic system disorders
Thrombocytopenia (some very rare cases were severe with platelet counts less than 5,000 per mm^3), lymphadenopathy

General disorders and administration site conditions
Extensive swelling of injected limb lasting more than one week, injection-site cellulitis-like reaction (some cases of swelling, pain, and redness extending more than 10 cm and lasting more than 1 week)

Immune system disorders
Allergic reactions including anaphylactic shock (in rare cases), anaphylaxis, and angioedema

Musculoskeletal and connective tissue disorders
Muscular weakness

Nervous system disorders
Encephalomyelitis, Guillain-Barré syndrome, convulsions, neuritis, neuralgia, paraesthesia

Skin and subcutaneous tissue disorders
Generalised skin reactions including erythema multiforme, urticaria, pruritus or non-specific rash

Vascular disorders
Vasculitis that may be associated with transient renal involvement

Paediatric population

There are no post-marketing data available for Fluad Tetra and limited data for Fluad (trivalent formulation) in the paediatric population.

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. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Overdosage is unlikely to have any untoward effect.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Influenza vaccine, ATC code: J07BB02

Mechanism of action

Fluad Tetra provides active immunisation against four influenza virus strains (two A subtypes and two B types) contained in the vaccine. Fluad Tetra induces humoral antibodies against the haemagglutinins. These antibodies neutralise influenza viruses.

Specific levels of haemagglutination inhibition (HI) antibody titres post-vaccination with inactivated influenza vaccine have not been correlated with protection from influenza virus, but the HI antibody titres have been used as a measure of vaccine efficacy.

Antibody against one influenza virus type or subtype confers limited or no protection against another. Furthermore, antibody to one antigenic variant of influenza virus might not protect against a new antigenic variant of the same type or subtype.

Fluad Tetra contains the adjuvant MF59C.1 (MF59), which is designed to increase and broaden the antigen-specific immune response and to extend the duration of the immune response.

Annual revaccination is recommended because immunity declines during the year after vaccination and circulating strains of influenza virus change from year to year.

Pharmacodynamic effects

Elderly population (65 years and older)

Immunogenicity
The immunogenicity of Fluad Tetra was evaluated in clinical study V118_20, a multicentre, randomised, double-blind, comparator controlled study conducted during the 2017-2018 Northern Hemisphere influenza season. Elderly subjects 65 years of age and older were randomised (2:1:1) to receive Fluad Tetra, the licensed adjuvanted trivalent influenza vaccine (Fluad, aTIV-1) or an adjuvanted trivalent influenza vaccine containing the alternate B strain (aTIV-2).
Eligible subjects were men or women ≥65 years of age who were healthy or had comorbidities that increased their risk of influenza complications. The mean age of subjects at enrolment who received Fluad Tetra was 72.4 years. Female subjects represented 58.2% of the study population.
The immunogenicity endpoints assessed 3 weeks after vaccination were haemagglutination inhibition (HI) geometric mean antibody titre (GMT) and HI seroconversion rate (pre-vaccination HI titre <1:10 and post-vaccination HI titre ≥ 1:40 or at least a 4-fold increase in HI from pre-vaccination HI titre

≥ 1:10). Fluad Tetra met non-inferiority for all 4 influenza strains and superiority to the alternate B strain not included in the Fluad aTIV comparators. The non-inferiority data are summarised in Table 2.

Table 2: Post-vaccination GMT and seroconversion rates in elderly subjects 65 years of age and older

	GMT (95% CI)			**GMT Ratio[a]**
Strain	**Fluad Tetra N=872**	**aTIV-1 (B-Victoria) N=436**	**aTIV-2 (B-Yamagata) N=433**	**aTIV[d]/Fluad Tetra (95% CI)**
A/H1N1	65.0 (57.8; 73.1)	75.2 (66.7; 84.7)		1.2 (1.1; 1.3)
A/H3N2	294.9 (261.9; 332.1)	293.3 (259.9; 331.0)		1.0 (0.9; 1.1)
B/Yamagata	24.7 (22.7; 26.8)	NA	24.3 (22.0; 26.8)	1.0 (0.9; 1.1)
B/Victoria	30.8 (28.3; 33.5)	30.1 (27.3; 33.2)	NA	1.0 (0.9; 1.1)
	Seroconversion %[c] (95% CI)			**Seroconversion Difference[b]**
Strain	**Fluad Tetra N=872**	**aTIV-1 (B-Victoria) N=436**	**aTIV-2 (B-Yamagata) N=433**	**aTIV[d] – Fluad Tetra (95% CI)**
A/H1N1	35.2 (32.0; 38.5)	38.4 (35.2; 41.8)		3.2 (-1.3; 7.8)
A/H3N2	39.3 (36.1; 42.7)	39.7 (36.4; 43.0)		0.4 (-4.2; 5.0)
B/Yamagata	16.4 (14.0; 19.0)	NA	15.5 (12.2; 19.2)	-0.9 (-5.1; 3.3)
B/Victoria	13.4 (11.2; 15.9)	12.2 (9.2; 15.6)	NA	-1.3 (-5.1; 2.6)

Abbreviations: GMT= Geometric Mean antibody titre; CI= Confidence Interval; NA= Not Applicable.
aTIV-1: licensed MF59-adjuvanted trivalent subunit inactivated egg-derived influenza vaccine, FLUAD TIV containing B-Victoria; aTIV-2: MF59-adjuvanted trivalent subunit inactivated egg-derived influenza vaccine containing B-Yamagata
N= the number of vaccinated subjects with available data from the immunogenicity endpoint listed (Per Protocol Set).
[a] Non-inferiority for the GMT ratio was defined as: the upper bound of the two-sided 95% CI for the ratio of the GMTs did not exceed 1.5.
[b] Non-inferiority for the seroconversion difference was defined as: the upper bound of the two-sided 95% CI for the difference between the seroconversions did not exceed 10%.
[c] Seroconversion was defined as pre-vaccination HI titre <1:10 and post-vaccination HI titre ≥ 1:40 or at least a 4-fold increase in HI from pre-vaccination HI titre ≥ 1:10.
[d] aTIV-1 and aTIV-2 vaccine groups are pooled for the analysis of A/H1N1 and A/H3N2 strains. For B/Victoria aTIV=aTIV-1, for B/Yamagata aTIV=aTIV-2.

Immunogenicity of aTIV

The immunogenicity of Fluad (trivalent formulation) is relevant to Fluad Tetra because both vaccines are manufactured using the same process and have overlapping compositions.
Study V70_27 was a large Phase 3, randomised, controlled, observer-blind, multicentre study to evaluate the immunogenicity and the safety of Fluad in comparison to non-adjuvanted vaccine and it was conducted in 2010-2011. Subjects were randomised in a 1:1 ratio to receive a single 0.5 ml dose of Fluad or a single dose of a non-adjuvanted influenza vaccine. All subjects were followed for approximately one year post-vaccination.

A total of 7082 subjects were randomised and vaccinated, including 3541 subjects in each of the pooled Fluad and non-adjuvanted vaccine groups. A total of 2573 subjects (1300 in Fluad and 1273 in non-adjuvanted vaccine group) were regarded as "high risk" subjects (underlying chronic diseases including congestive heart failure, chronic obstructive pulmonary disease, asthma, hepatic disease, renal insufficiency and/or neurological/neuromuscular or metabolic disorders including diabetes mellitus).
The primary objective of a superiority of Fluad versus non-adjuvanted vaccine was not achieved for all homologous strains. GMT ratios ranged from 1.15 to 1.61 with the lowest limit of the 95% CI of 1.08 and differences in seroconversion rates ranged from 3.2% – 13.9% with the lowest limit of the 95% CI of 1.1%.
Fluad elicited higher antibody titres for A/H3N2 that persisted up to 12 months post-vaccination. The results were similar for high-risk subjects with predefined comorbidities.

Effectiveness
No effectiveness studies have been performed with Fluad Tetra. The observational effectiveness studies performed with Fluad (trivalent formulation) are relevant to Fluad Tetra because both vaccines are manufactured using the same process and have overlapping compositions.

Paediatric Population (6 months to less than 6 years)

Fluad Tetra is not indicated for use in children, see section 4.2.
Efficacy, immunogenicity and safety of Fluad Tetra was evaluated in clinical study V118_05, a multicentre, randomised, observer-blinded, controlled study conducted in the 2013-14 (season 1) and 2014-15 (season 2) Northern Hemisphere seasons in children of 6 months to less than 6 years. Children less than 3 years of age received 0.25 ml vaccine, older children received 0.5 ml vaccine. Children naïve to prior influenza vaccination received two doses of vaccine, at least 4 weeks apart. 10,644 children were enrolled and randomised to receive Fluad Tetra or the non-adjuvanted comparator vaccine in a 1:1 ratio: 5,352 children were enrolled in the Fluad Tetra group and 5,292 children in the non-adjuvanted comparator vaccine group.

Immunogenicity

A subset of children enrolled in this study was evaluated for their immunological response to Fluad Tetra and the non-adjuvanted comparator. Immunogenicity assessments were performed prior to (each) vaccination and 3 weeks after the last vaccination. A total of 2886 children were included in the subset for immunogenicity evaluation (Fluad Tetra: N=1481; non-adjuvanted comparator vaccine: N=1405).

Fluad Tetra demonstrated a higher immune response compared to the non-adjuvanted comparator vaccine. In addition, in children naïve to influenza vaccination antibody titres 4 weeks after the first vaccination as well as 3 weeks after the second vaccination were greater in subjects who received Fluad Tetra.
At 12 months post-vaccination, persistence of the immune response was higher in the Fluad Tetra group compared to the non-adjuvanted comparator group.

Efficacy

Vaccine efficacy was assessed for the prevention of first-occurrence laboratory confirmed influenza associated with symptomatic influenza-like illness (ILI). Influenza-like illness was defined as fever of 37.8°C or above along with any of the following: cough, sore throat, nasal congestion, or runny nose occurring at ≥ 21 days and ≤ 180 days after the last vaccination or until the end of the influenza season, whichever was longer. Subjects with ILI had nasopharyngeal swabs collected and tested for influenza A (A/H1N1 and A/H3N2) and B (both lineages) by Reverse Transcription-Polymerase Chain Reaction (RT-PCR). A total of 508 cases of first-occurrence RT-PCR confirmed influenza occurred during the study; 10 during season one and 498 during season two. The majority of influenza cases were A/H3N2. Based on antigenic typing, more than ninety percent of A/H3N2 strains from

season two were determined to be antigenically distinct from egg-propagated A/Texas/50/2012, the H3N2 vaccine strain.

Vaccine efficacy compared to the non-adjuvanted influenza comparator vaccine was assessed. The relative vaccine (rVE) efficacy between Fluad Tetra and the comparator vaccine group in subjects ≥6 to <72 months of age was -0.67 [95% CI: -19.81; 15.41]), which did not meet the primary objective of the study.

Safety

Safety data were collected up to 12 months after receipt of the last vaccination.
A higher incidence of local and systemic reactions was reported in subjects who received Fluad Tetra compared to the non-adjuvanted comparator influenza vaccine.

The most commonly reported adverse reactions (≥10%) were tenderness (43.2%), irritability (27.1%), sleepiness (26.3%), change in eating habits (22.5%), fever (19.1%), diarrhoea (12.3%) and vomiting (10.3%).

The European Medicines Agency has deferred the obligation to submit the results of studies with Fluad Tetra in one or more subsets of the paediatric population in prevention of influenza infection. See section 4.2 for information on paediatric use.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated-dose toxicity, reproductive and developmental toxicity, local tolerance and sensitisation.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

For adjuvant: see also section 2.

Sodium chloride
Potassium chloride
Potassium dihydrogen phosphate
Disodium phosphate dihydrate
Magnesium chloride hexahydrate
Calcium chloride dihydrate
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

12 months

6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C). Do not freeze. Discard if the vaccine has been frozen.
Keep the pre filled syringe in the outer carton in order to protect from light.

6.5 Nature and contents of container

0.5 ml of suspension for injection in pre-filled syringe (type I glass) with a plunger stopper (bromobutyl rubber), presented with or without needle.

Pack of 1 pre-filled syringe with needle
Pack of 1 pre-filled syringe without needle
Pack of 10 pre-filled syringes with needles
Pack of 10 pre-filled syringes without needles

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Gently shake before use.
After shaking, the normal appearance of the vaccine is a milky-white suspension.

Visually inspect the contents of each pre-filled syringe for particulate matter and/or variation in appearance prior to administration. If either condition is observed, do not administer the vaccine. Do not use if the vaccine has been frozen. Any unused product or waste material should be disposed of in accordance with local requirements.

When using a pre-filled syringe supplied without a needle, remove the tip cap from the syringe and then attach a suitable needle for administration. For Luer Lock syringes, remove the tip cap by unscrewing it in a counter-clockwise direction. Once the tip cap is removed, attach a needle to the syringe by screwing it on in a clockwise direction until it locks. Once the needle is locked in place, remove the needle protector and administer the vaccine.

7. MARKETING AUTHORISATION HOLDER

Seqirus Netherlands B.V.
Paasheuvelweg 28
1105 BJ Amsterdam
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1433/001
EU/1/20/1433/002
EU/1/20/1433/003
EU/1/20/1433/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: DD month YYYY

10. DATE OF REVISION OF THE TEXT

MM/YYYY

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) of the biological active substance(s)

Seqirus Vaccines Limited
Gaskill Road, Speke
L24 9GR Liverpool
United Kingdom

Name and address of the manufacturer(s) responsible for batch release

Seqirus Vaccines Limited
Gaskill Road, Speke
L24 9GR Liverpool
United Kingdom

Seqirus Netherlands B.V.
Paasheuvelweg 28
1105 BJ Amsterdam
Netherlands

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

- **Official batch release**

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic Safety Update Reports (PSURs)**

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

Carton box for syringe(s) with or without needle
- 1 pre-filled syringe (0.5 ml) with needle
- 1 pre-filled syringe (0.5 ml) without needle
- 10 pre-filled syringes (0.5 ml) with needle
- 10 pre-filled syringes (0.5 ml) without needle

1. NAME OF THE MEDICINAL PRODUCT

Fluad Tetra, suspension for injection in pre-filled syringe
Influenza vaccine (surface antigen, inactivated, adjuvanted)
xxxx/xxxx season

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Influenza virus surface antigens (haemagglutinin and neuraminidase), inactivated, of the following strains per 0.5 ml dose:

A/xxxxx (H1N1) - like strain	15 micrograms HA*
A/xxxxx (H3N2) - like strain	15 micrograms HA*
B/xxxxx - like strain	15 micrograms HA*
B/xxxxx – like strain	15 micrograms HA*

* haemagglutinin

3. LIST OF EXCIPIENTS

Adjuvant MF59C.1: squalene, polysorbate 80, sorbitan trioleate, sodium citrate, citric acid

Excipients: sodium chloride, potassium chloride, potassium dihydrogen phosphate, disodium phosphate dihydrate, magnesium chloride hexahydrate, calcium chloride dihydrate, water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection in pre-filled syringe

1 pre-filled syringe (0.5 ml) with needle
1 pre-filled syringe (0.5 ml) without needle
10 pre-filled syringes (0.5 ml) with needle
10 pre-filled syringes (0.5 ml) without needle

5. METHOD AND ROUTE OF ADMINISTRATION

Intramuscular use.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

65 years and older

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in refrigerator. Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Seqirus Netherlands B.V.
Paasheuvelweg 28
1105 BJ Amsterdam
Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1433/001
EU/1/20/1433/002
EU/1/20/1433/003
EU/1/20/1433/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

Gently shake before use

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Pre-filled syringe label
- pre-filled syringe (0.5 ml) with needle
- pre-filled syringe (0.5 ml) without needle

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE OF ADMINISTRATION

Fluad Tetra injection
Influenza vaccine
xxxx/xxxx season

2. METHOD OF ADMINISTRATION

IM

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Fluad Tetra, suspension for injection in pre-filled syringe
Influenza vaccine (surface antigen, inactivated, adjuvanted)

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you receive this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Fluad Tetra is and what it is used for

Fluad Tetra is a vaccine against flu (influenza).
When a person is given the vaccine, the immune system (the body's natural defence system) will produce its own protection against the influenza virus. None of the ingredients in the vaccine can cause flu.

Fluad Tetra is used to prevent flu in elderly adults of 65 years of age and older.

The vaccine targets four strains of influenza virus following the recommendations by the World Health Organisation for the xxxx/xxxx season.

2. What you need to know before you receive Fluad Tetra

You should not receive Fluad Tetra
- if you are allergic to
  - the active ingredients or any of the other ingredients of this medicine (listed in section 6)
  - egg or chicken proteins (such as ovalbumin), kanamycin and neomycin sulphate, formaldehyde, cetyltrimethylammonium bromide (CTAB) and hydrocortisone, which are trace residues from the manufacturing process.
- If you have had a severe allergic reaction (e.g. anaphylaxis) to previous influenza vaccination.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before receiving Fluad Tetra

<u>BEFORE receiving the vaccine</u>
- Your doctor or nurse will make sure that appropriate medical treatment and supervision is readily available in case of a rare anaphylactic reaction (a very severe allergic reaction with symptoms

such as difficulty in breathing, dizziness, a weak and rapid pulse and skin rash) following the administration. This reaction may occur with Fluad Tetra as with all vaccines that are injected.
- You should tell your doctor if you have an acute illness associated with fever. Your doctor may decide to delay your vaccination until your fever is gone.
- You should tell your doctor if your immune system is impaired, or if you are undergoing treatment which affects the immune system, e.g. with medicine against cancer (chemotherapy) or corticosteroid medicines (see Section "Other medicines and Fluad Tetra").
- You should tell your doctor if you have a bleeding problem or bruise easily.
- Fainting can occur following, or even before, any needle injection, therefore tell the doctor or nurse if you fainted with a previous injection.

As with all vaccines, Fluad Tetra may not fully protect all persons who are vaccinated.

Children
Fluad Tetra is not recommended for use in children.

Other medicines and Fluad Tetra
Tell your doctor or nurse if you are using, have recently used or might use any other medicines, including medicines obtained without a prescription or if you have recently received any other vaccine.

Pregnancy and breast-feeding
This vaccine is for use in elderly adults 65 years and older. It is not to be used in women who are, or may be, pregnant or breast-feeding.

Driving and using machines
Fluad Tetra has no or negligible influence on the ability to drive and use machines.

Fluad Tetra contains potassium and sodium
This vaccine contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium free'.
This vaccine contains potassium, less than 1 mmol (39 mg) per dose, i.e. essentially 'potassium free'.

3. How Fluad Tetra is given

Fluad Tetra is given by your doctor or nurse as an injection into the muscle at the top of the upper arm (deltoid muscle).

Adults of 65 years of age and older:

One dose of 0.5 ml

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects have been reported during clinical trials in adults 65 years of age and older.

Mild side effects
Very common (may affect more than 1 in 10 people):
- Pain at injection site
- Fatigue
- Headache

Common (may affect up to 1 in 10 people):
- Joint pain (arthralgia)
- Muscular pain (myalgia)
- Redness at injection site (erythema)
- Hardening of the skin at injection site (induration)
- Diarrhoea
- Shivering
- Nausea
- Loss of appetite
- Bruising at injection site (ecchymosis)
- Flu-like symptoms

Uncommon (may affect up to 1 in 100 people):
- Vomiting
- Fever (≥ 38°C)

Most side effects were mild or moderate and went away within 3 days of appearing.

Next to the above side effects, the following side effects occurred occasionally during general use of another vaccine similar to Fluad Tetra.
- reduction in the number of certain types of particles in the blood called platelets; a low number of these can result in excessive bruising or bleeding (thrombocytopenia); swelling of the glands in the neck, armpit or groin (lymphadenopathy)
- swelling, pain and redness at the injection site extending to more than 10 cm and lasting more than one week (Injection site cellulitis-like reaction)
- extensive swelling of injected limb lasting more than one week.
- allergic reactions:
  - sudden fall in blood pressure due to severe allergic reactions that in rare cases can lead to failure of the circulatory system to maintain adequate blood flow to the different organs (shock),
  - swelling most apparent in the head and neck, including the face, lips, tongue, throat or any other part of the body (angioedema).
- muscular weakness
- pain on the nerve path (neuralgia), unusual feeling of touch, pain, heat and cold (paraesthesia), fits (convulsions), neurological disorders that may result in stiff neck, confusion, numbness, pain and weakness of the limbs, loss of balance, loss of reflexes, paralysis of part or all the body (encephalomyelitis, neuritis, Guillain-Barré Syndrome)
- skin reactions that may spread throughout the body including itchiness of the skin (pruritus, urticaria), rash
- severe skin rash (erythema multiforme)
- blood vessel swelling that may cause skin rashes (vasculitis) and temporary kidney problems

Reporting of side effects
If you get any side effects, talk to your health care professional. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Fluad Tetra

Keep this medicine out of the sight and reach of children.

Store in a refrigerator (2 °C to 8 °C). Do not freeze. Discard if the vaccine has been frozen.
Keep the pre-filled syringe in the outer carton in order to protect from light.

Do not use this medicine after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Fluad Tetra contains

The active substances are:
Influenza virus surface antigens (haemagglutinin and neuraminidase), inactivated, of the following strains*:

	per 0.5 ml dose
A/xxxxx (H1N1) - like strain (*reassortant used*)	15 micrograms HA**
A/xxxxx (H3N2) - like strain (*reassortant used*)	15 micrograms HA**
B/xxxxx – like strain (*reassortant used*)	15 micrograms HA**
B/xxxxx – like strain (*reassortant used*)	15 micrograms HA**

*propagated in fertilised hens' eggs from healthy chicken flocks and adjuvanted with MF59C.1
**haemagglutinin

This vaccine complies with the WHO recommendations (Northern Hemisphere) and EU recommendation for the xxxx/xxxx season.

MF59C.1 is included in this vaccine as an adjuvant. Adjuvants are substances included in certain vaccines to accelerate, improve and/or prolong the protective effects of the vaccine. MF59C.1 is an adjuvant that contains per 0.5 ml dose: squalene (9.75 mg), polysorbate 80 (1.175 mg), sorbitan trioleate (1.175 mg), sodium citrate (0.66 mg) and citric acid (0.04 mg).

The other ingredients are:
sodium chloride, potassium chloride, potassium dihydrogen phosphate, disodium phosphate dihydrate, magnesium chloride hexahydrate, calcium chloride dihydrate and water for injections.

What Fluad Tetra looks like and contents of the pack

Fluad Tetra is a suspension for injection in a pre-filled (ready to use) syringe. Fluad Tetra is a milky-white suspension. A single syringe contains 0.5 ml of suspension for injection. Fluad Tetra is available in packs containing 1 or 10 pre-filled syringes with or without needles.
Not all pack sizes may be marketed.

Marketing Authorisation Holder

Seqirus Netherlands B.V.
Paasheuvelweg 28
1105 BJ Amsterdam
Netherlands

Manufacturers

Seqirus Vaccines Limited
Gaskill Road, Speke
L24 9GR Liverpool
United Kingdom

Seqirus Netherlands B.V.
Paasheuvelweg 28
1105 BJ Amsterdam
Netherlands

This leaflet was last revised in {MM/YYYY}.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

The following information is intended for healthcare professionals only:

Appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

Gently shake before use. After shaking, the normal appearance of the vaccine is a milky white suspension.

The vaccine should be visually inspected for particulate matter and discoloration prior to administration. In the event of any foreign particulate matter and/or variation of physical aspect being observed, do not administer the vaccine.

When using a pre-filled syringe supplied without a needle, remove the tip cap from the syringe and then attach a suitable needle for administration. For Luer Lock syringes, remove the tip cap by unscrewing it in a counter-clockwise direction. Once the tip cap is removed, attach a needle to the syringe by screwing it on in a clockwise direction until it locks. Once the needle is locked in place, remove the needle protector and administer the vaccine.