ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Fluad 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/Victoria/4897/2022 (H1N1)pdm09-like strain (A/Victoria/4897/2022 IVR-238)	15 micrograms HA**
A/Darwin/9/2021 (H3N2) like strain (A/Darwin/6/2021 IVR-227)	15 micrograms HA**
B/Austria/1359417/2021-like strain (B/Austria/1359417/2021 BVR-26)	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 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 adults 50 years of age and older.

Fluad 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 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.

Hypersensitivity and anaphylaxis

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

Concurrent illness

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

Thrombocytopenia and coagulation disorders

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

Anxiety-related reactions

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.

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

Limitations of vaccine effectiveness

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

Excipients with known effect

Sodium

This vaccine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

Potassium

This vaccine contains potassium, less than 1 mmol (39 mg) per dose, that is to say essentially 'potassium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

No clinical data on concomitant administration of Fluad with other vaccines are available. If Fluad 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 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 has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Data for the adjuvanted quadrivalent influenza vaccine (Fluad Tetra) are relevant to Fluad because both vaccines are manufactured using the same process and have overlapping compositions.

Summary of the safety profile

Safety in adults 50 to less than 65 years of age, and elderly 65 years of age and older was assessed in 4 clinical studies. In these studies, 9 729 subjects received Fluad (N=3 545, Study V70_27), an adjuvanted quadrivalent influenza vaccine (N=5 296, Studies V118_18, V118_20 and V118_23) or one of two formulations of an adjuvanted trivalent comparator (N=888).

The most commonly reported (≥10%) adverse reactions in adults 50 to less than 65 years of age who received adjuvanted quadrivalent influenza vaccine were injection site pain (47%), fatigue (30%), headache (22%), arthralgia (14%) and myalgia (13%).

The most commonly reported (≥10%) adverse reactions in subjects 65 years of age who received Fluad, adjuvanted quadrivalent influenza vaccine or adjuvanted trivalent comparators were injection site pain (32%), injection site tenderness (21%), fatigue (16%), myalgia (15%) and headache (13%).

Most reactions were reported as mild or moderate in intensity and resolved within the first 3 days after vaccination.

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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); Frequency not known.

Table 1: Adverse reactions reported following vaccination in adult subjects 50 years and older in clinical trials and post-marketing surveillance

MedDRA System Organ class	Very common (≥1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)	Frequency not known[4]
Blood and lymphatic system disorders			Lymphadenopathy	Thrombocytopenia (some very rare cases were severe with platelet counts less than 5,000 per mm^3)
Immune system disorders				Allergic reactions including anaphylactic shock (in rare cases), anaphylaxis
Metabolism and nutrition disorders		Loss of appetite		
Nervous system disorders	Headache			Encephalomyelitis, Guillain-Barré syndrome, convulsions, neuritis, neuralgia, paraesthesia, syncope, presyncope
Vascular disorders				Vasculitis that may be associated with transient renal involvement
Gastrointestinal disorders		Nausea, diarrhoea	Vomiting	
Skin and subcutaneous tissue disorders				Generalised skin reactions including erythema multiforme, erythema, urticaria, pruritus or non-specific rash, angioedema
Musculoskeletal and connective tissue disorders	Myalgia[1], arthralgia[1]			Muscular weakness, pain in extremity
General disorders and administration site conditions	Injection site pain/tenderness, fatigue	Ecchymosis*, chills, erythema, induration, influenza-like illness[2], fever (≥38°C)[3]		Extensive swelling of injected limb lasting more than one week, injection-site cellulitis-like reaction, asthenia, malaise, pyrexia

*Or Injection site bruising

[1] Reported as Common (≥1/100 to <1/10) in elderly subjects 65 years and older

[2] Unsolicited adverse reaction reported in elderly subjects 65 years and older

[3] Reported as Uncommon (≥1/1,000 to <1/100) in elderly subjects 65 years and older

[4] Adverse reactions reported from post-marketing surveillance for adjuvanted quadrivalent influenza vaccine or Fluad

Paediatric population

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

There are limited post-marketing data for Fluad 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 provides active immunisation against the influenza virus strains contained in the vaccine. Fluad 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 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 with influenza vaccines is recommended because immunity declines during the year after vaccination and circulating strains of influenza virus may change from year to year.

Pharmacodynamic effects

Immunogenicity in the elderly population 65 years of age and older

Study V70_27 was a large Phase 3, randomised, controlled, observer-blind, multi-centre study conducted in 2010-2011 to evaluate the immunogenicity, the safety and the consistency of three consecutive lots of Fluad in comparison to non-adjuvanted vaccine. Subjects were randomised in a 1:1:1:3 ratio to receive a single 0.5 mL dose of 1 of 3 consecutive lots of Fluad or a single lot of a non-adjuvanted influenza vaccine. All subjects were followed for approximately one year post-vaccination.

A total of 7 082 subjects were randomised and vaccinated, including 3 541 subjects in each of the pooled Fluad and non-adjuvanted vaccine groups. A total of 2 573 subjects (1 300 in Fluad and 1 273 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 superiority of Fluad versus non-adjuvanted vaccine was not achieved for all homologous strains; the co-primary objective of non-inferiority of Fluad versus non-adjuvanted vaccine was achieved for all homologous strains; however significantly higher HI titre rates against all three homologous strains of influenza at day 22 post vaccination were seen in subjects that received Fluad compared with non-adjuvanted influenza vaccine (Table 2). The results were similar for high-risk subjects with predefined comorbidities.

In addition, in a subset of subjects (n=1 649 subjects), Fluad was compared to the non-adjuvanted influenza vaccine for heterologous strains, i.e. influenza variants of the same type/subtype that were not included in the vaccine composition (secondary objective). Superiority of Fluad as compared to non-adjuvanted influenza vaccine was not achieved for all 3 heterologous strains at day 22; however non-inferiority was demonstrated for all 3 heterologous strains at day 22. Results were similar for high-risk subjects (609 subjects).

Table 2: Postvaccination GMTs and Vaccine Group Ratios – HI assay

Study	Antigen	Fluad		Non-adjuvanted Vaccine		
		N	GMT (95% CI)	N	GMT (95% CI)	Vaccine Group Ratio (95% CI)
All subjects[a]	H3N2	3225	272 (257-288)	3256	169 (159-179)	1.61 (1.52-1.7)[§]
	H1N1	3225	99 (93-106)	3257	70 (66-75)	1.4 (1.32-1.49)[§]
	B	3227	28 (26-29)	3259	24 (23-26)	1.15 (1.08-1.21)[§]
High-risk subjects[a]	H3N2	1194	260 (238-283)	1190	165 (152-180)	1.57 (1.44-1.72)[§]
	H1N1	1194	110 (100-122)	1190	80 (73-88)	1.38 (1.25-1.52)[§]
	B	1195	30 (28-33)	1190	27 (25-29)	1.12 (1.03-1.22)[§]

HI: Hemagglutination inhibition assay; GMT: Geometric Mean HI titers; CI: Confidence Interval
[a] Postvaccination (Day 22) GMTs and vaccine group GMT ratios (Fluad: non-adjuvanted influenza vaccine) are adjusted for baseline titre, country and age cohort; Per Protocol Population.
[§] As the lower limit of the 95% CI of the vaccine group ratio is greater than 1, it is regarded that HI titres after vaccination with Fluad are higher than those of the non-adjuvanted influenza vaccine.

Immunogenicity of adjuvanted quadrivalent influenza vaccine in the adult population 50 to less than 65 years of age

Data for adjuvanted quadrivalent influenza vaccine are relevant to Fluad because both vaccines are manufactured using the same process and have overlapping compositions.

Immunogenicity of adjuvanted quadrivalent influenza vaccine in adults 50 to less than 65 years of age was evaluated in Study V118_23. This was a randomised, observer-blind, controlled, multi-centre clinical study conducted in the US, Germany and Estonia, during the 2021-22 Northern Hemisphere season. In this study, adults 50 to less than 65 years of age who were healthy or had comorbidities that increased their risk of hospitalisation for influenza-associated complications, were enrolled to receive one dose of either adjuvanted quadrivalent influenza vaccine (N=1027) or a non-adjuvanted

quadrivalent comparator influenza vaccine (N=1017). The mean age of subjects enrolled in the adjuvanted quadrivalent influenza vaccine group was 57.8 years and females represented 62% of subjects.

The immunogenicity endpoints assessed 3 weeks after vaccination were HI 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). As was seen in studies in older adults with aTIV (see above study V70_27), adjuvanted quadrivalent influenza vaccine elicited higher immune responses compared to a non-adjuvanted quadrivalent comparator influenza vaccine although superiority of adjuvanted quadrivalent influenza vaccine versus non-adjuvanted vaccine was not achieved for all four homologous strains. The HI GMT ratios (comparator/ adjuvanted quadrivalent influenza vaccine) ranged from 0.80 to 0.99 with the highest limit of the 95% CI of 1.07 and differences in HI seroconversion rates (comparator – adjuvanted quadrivalent influenza vaccine) ranged from -4.5% to -1.8% with the highest limit of the 95% CI of 2.5%.

Paediatric Population (6 months to less than 6 years)

Fluad is not indicated for use in children, see section 4.2.
Efficacy, immunogenicity and safety of adjuvanted quadrivalent influenza vaccine was evaluated in clinical study V118_05, a multi-centre, 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 adjuvanted quadrivalent influenza vaccine or the non-adjuvanted comparator vaccine in a 1:1 ratio: 5,352 children were enrolled in the adjuvanted quadrivalent influenza vaccine group and 5,292 children in the non-adjuvanted comparator vaccine group.

Immunogenicity in the paediatric population

A subset of children enrolled in this study was evaluated for their immunological response to adjuvanted quadrivalent influenza vaccine 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 (adjuvanted quadrivalent influenza vaccine: N=1481; non-adjuvanted comparator vaccine: N=1405).

Adjuvanted quadrivalent influenza vaccine 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 adjuvanted quadrivalent influenza vaccine.

At 12 months post-vaccination, persistence of the immune response was higher in the adjuvanted quadrivalent influenza vaccine group compared to the non-adjuvanted comparator group.

Efficacy in the paediatric population

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 adjuvanted quadrivalent influenza vaccine 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.

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, toxicity to reproduction and development, 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

1 year

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. Each pre-filled syringe contains one dose of 0.5 ml.

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

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 medicinal 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 needle for administration. Use a sterile needle of the appropriate size for intramuscular injection. 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/1/24/1878/001
EU/1/24/1878/002
EU/1/24/1878/003
EU/1/24/1878/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

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 Netherlands B.V.
Paasheuvelweg 28
1105 BJ Amsterdam
Netherlands

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 PSURs 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 marketing authorisation holder (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, suspension for injection in pre-filled syringe
Influenza vaccine (surface antigen, inactivated, adjuvanted)
XXXX/XXXX SEASON

2. STATEMENT OF ACTIVE SUBSTANCE(S)

XXXX/XXXX SEASON

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

A/Victoria/4897/2022 (H1N1)pdm09-like strain	15 micrograms HA*
A/Darwin/9/2021 (H3N2)-like strain	15 micrograms HA*
B/Austria/1359417/2021-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. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection

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

50 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/1/24/1878/001
EU/1/24/1878/002
EU/1/24/1878/003
EU/1/24/1878/004

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 injection
Influenza vaccine
XXXX/XXXX Season

IM

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 ml
15 mcg HA per strain/dose

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

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

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 is and what it is used for

Fluad 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 is used to prevent flu in adults 50 years of age and older.

The vaccine targets 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

You should not receive Fluad
- if you are allergic to
  - the active substances 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.

<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 as with all vaccines that are injected.
- You should tell your doctor if you have an 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").
- 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 may not fully protect all persons who are vaccinated.

Children
Fluad is not recommended for use in children.

Other medicines and Fluad
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 adults 50 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 has no or negligible influence on the ability to drive and use machines.

Fluad 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 is given

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

Adults 50 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.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you experience the following serious side effect – you may need urgent medical attention or hospitalisation:

- Difficulty in breathing, dizziness, a weak and rapid pulse and skin rash which are symptoms of an anaphylactic reaction (a very severe allergic reaction)

The following side effects have been reported during clinical trials in adults 50 years of age and older.

Very common (may affect more than 1 in 10 people):
- Pain or tenderness at injection site
- Fatigue
- Headache
- Joint pain (arthralgia)[1]
- Muscular pain (myalgia)[1]

[1] reported as Common in elderly subjects 65 years of age and older

Common (may affect up to 1 in 10 people):
- 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[2]
- Fever (≥ 38°C)[3]

[2] reported in elderly subjects 65 years of age and older
[3] reported as Uncommon in elderly subjects 65 years of age and older

Uncommon (may affect up to 1 in 100 people):
- Vomiting
- Swelling of the glands in the neck, armpit or groin (lymphadenopathy)

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 adjuvanted quadrivalent influenza vaccine or Fluad.
- 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, pain and redness at the injection site (injection site cellulitis-like reaction)
- extensive swelling of injected limb lasting more than one week
- general weakness or lack of energy (asthenia), generally feeling unwell (malaise)
- fever (pyrexia)
- muscular weakness
- pain on the nerve path (neuralgia), unusual feeling of touch, pain, heat and cold (paraesthesia), fits (convulsions), ne urological 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), skin redness (erythema), non-specific rash, severe skin rash (erythema multiforme)
- swelling most apparent in the head and neck, including the face, lips, tongue, throat or any other part of the body (angioedema)
- blood vessel swelling that may cause skin rashes (vasculitis) and temporary kidney problems
- fainting, feeling about to faint (syncope, presyncope)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. 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

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 contains

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

	per 0.5 ml dose
A/Victoria/4897/2022 (H1N1)pdm09-like strain (A/Victoria/4897/2022 IVR-238)	15 micrograms HA**
A/Darwin/9/2021 (H3N2)-like strain (A/Darwin/6/2021 IVR-227)	15 micrograms HA**
B/Austria/1359417/2021-like strain (B/Austria/1359417/2021 BVR-26)	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 looks like and contents of the pack
Fluad is a suspension for injection in a pre-filled syringe. Fluad is a milky-white suspension. Each pre-filled syringe contains a single dose (0.5 ml) of suspension for injection. Fluad 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 and Manufacturer
Seqirus Netherlands B.V.
Paasheuvelweg 28,1105 BJ Amsterdam, Netherlands

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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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 needle for administration. Use a sterile needle of the appropriate size for intramuscular injection. 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.