1. NAME OF MEDICINAL PRODUCT

3Fluart suspension for injection
influenza vaccine (whole virus, inactivated, adjuvanted)
(for the season of 2018/2019)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

The composition of 1 dose (0.5 ml) of vaccine for the 2017/2018 season is as follows:

The vaccine contains a formaldehyde-inactivated whole virion* with the following antigen composition:

A/Michigan/45/2015 (H1N1)pdm09-like strain (A/Michigan/45/2015, NYMC X-275)	6 µg HA**
A/Singapore/INFIMH-16-0019/2016 (H3N2)-like strain (A/Singapore/INFIMH-16-0019/2016, IVR-186)	6 µg HA**
B/Colorado/06/2017-like strain (B/Maryland/15/2016, NYMC BX-69A)	6 µg HA**

* propagated in embryonated hens' eggs
** haemagglutinin

This vaccine composition complies with the World Health Organisation (WHO) recommendation (northern hemisphere) and EU recommendation for the 2018/2019 season.

A single dose contains a maximum of 1µg ovalbumin, 0.5 µg gentamicin, neomycin, vancomycin and ciprofloxacin.

Adjuvant: aluminum-phosphate gel (max. 0.625 milligram Al^{3+})

Excipients of known effect: Thiomersal (max. 53 microgram)

For the full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.
Off-white, slightly opalescent suspension.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Prohylaxis of influenza from age 3.

It is especially recommended in those who run an increased risk of associated complications.

The vaccine provides protection against diseases caused by influenza strains whose antigen structure is similar to or identical with the prototype strains of the vaccine. The vaccine does not provide protection against influenza-like diseases caused by other pathogens.

The use of 3Fluart suspension for injection should be based on official recommendations.

4.2 Posology and method of administration

Posology

Adults and elderly: 1×0.5 ml

Paediatric population
Adolescents above 12 years: 1×0.5 ml
Children between 3-11 years of age: 1×0.25 ml

The safety and efficacy of 3Fluart vaccine in children under 3 years have not been established.

Immunisation should be carried out by single injection.

Method of administration

The vaccine should be administered intramuscularly, in the deltoid muscle of the upper arm, by means of the supplied sterile safety syringe and needle after careful disinfection of the injection site.

For children aged 3-11 years: the total volume of the homogenized vaccine should be drawn up into the supplied sterile safety syringe and needle then, by holding the syringe upright, a portion of the vaccine should be expelled out of the syringe so that exactly 0.25 ml of the vaccine remains in the syringe. Inject the remaining 0.25 ml content of the syringe intramuscularly after skin disinfection, into the deltoid muscle of the upper arm.

The immune response develops in approximately 2-3 weeks and lasts for several months. Therefore, vaccination is best administered before the epidemic period.

Precautions to be taken before handling or administering the medicinal product

3Fluart suspension for injection should under no circumstances be administered intravascularly. No intravascular administration of the vaccine is allowed.

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

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1, such as thiomersal, or any component that may be present in traces, such as egg (ovalbumin), formaldehyde, gentamicin, neomycin, vancomycin or ciprofloxacin.

Serious complications in the medical history with regard to any previous vaccination: encephalitis/encephalopathy, nonfebrile seizures, Guillain-Barré syndrome, vasculitis, neuritis, facial paresis.

Immunisation shall be postponed in patients with febrile illness or acute infection with 2-3 days after the symptoms disappear.

Contraindicated in children under 3 years of age (see section 4.2).

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 event following the administration of the vaccine.

The 3Fluart suspension for injection should under no circumstances be administered intravascularly.

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

The vaccine should be administered with increased caution in patients with known increased susceptibility to febrile seizure since febrile conditions may appear as an undesirable effect of vaccination. In such cases increased monitoring of the patients after vaccination and prevention of fever is recommended.

4.5 Interaction with other medicinal products and other forms of interaction

Based on the results of clinical trials on adults (over 18 years of age) seasonal and pandemic vaccine of the manufacturer can be given at the same time. Immunisation should be carried out on separate limbs.

The immunological response may be diminished 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.

Paediatric population

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy

The limited data from vaccinations in pregnant women do not indicate that adverse fetal and maternal outcomes were attributable to the vaccine.
Vaccination of pregnant women is recommended only after careful evaluation of the influenza and associated complications and the undesirable effects of the vaccination.

Breastfeeding

The 3Fluart suspension for injection can be used during breast-feeding.

Fertility

No fertility data are available.

4.7 Effects on ability to drive and use machines

3Fluart suspension for injection has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

As the vaccine contains inactivated virion, influenza infection cannot be caused by vaccination.
Any respiratory disease after vaccination is only a coincidence and is caused by another respiratory pathogen. The most common adverse reaction following injection is erythema (redness of the skin) or vaccination site pain, which usually disappears within 48 hours.

Adverse reactions observed from clinical trials

Frequency of reported side effects:
Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1000 to <1/100); Rare (≥1/10 000 to <1/1000); Very rare (<1/10 000); Not known (cannot be estimated from the available data)

System Organ Class *Frequency*	**Adverse reactions (Preferred terms)**
Nervous system disorders	
Common	Headache
Rare	Dizziness Hypoesthesia (numbness in arm, vaccination site numbness)
Respiratory, thoracic and mediastinal disorders	
Not known	Dysphonia
Gastrointestinal disorders	
Rare	Nausea
Musculoskeletal and connective tissue disorders	
Common	Myalgia
Uncommon	Arthralgia Pain in extremity
Skin and subcutaneous tissue disorders	
Rare	Urticaria
Not known	Erythema (redness of former vaccination, increase of existing papilla)
General disorders and administration site conditions	
Very common	Vaccination site pain
Common	Vaccination site erythema, swelling, induration Pyrexia/Fever Malaise
Uncommon	Vaccination site haematoma Chills Fatigue
Rare	Hyperhydrosis
Not known	Pallor

Paediatric population

Frequency of adverse effects reported in clinical trials in children and adolescents above 3 years is the same as in adults.

Adverse reactions reported from post-marketing surveillance

Data are available for seasonal influenza vaccine containing higher dose of virus than the 3Fluart vaccine. In addition to the above, the following adverse reactions have been reported:

Immune system disorders:
Allergic reactions

Nervous system disorders:
Parsonage-Turner syndrome*, paresis*, IVth nerve paralysis*

Skin and subcutaneous tissue disorders:
Burning sensation, pruritus, rash

Investigations
Platelet count decreased (in patients with idiopathic thrombocytopenic purpura)

General disorders and administration site conditions:
Asthenia, vaccination site warmth

* the above adverse events occurred upon co-administration with pandemic monovalent influenza vaccine.

Other possible complications according to literature include neuritis, encephalopathy, Guillain-Barré syndrome (GBS), and Gianotti-Crosti syndrome.

The vaccine contains thiomersal (organomercuric compound) as a preservative and therefore it is possible that sensitisation reactions may occur (see section 4.3).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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

No data are available on the overdosage of the vaccine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Influenza vaccine, ATC code: J07BB01

Seroloprotection is generally obtained within 2 to 3 weeks. The duration of postvaccinal immunity to homologuous strains or to strains closely related to the vaccine strains varies but is usually several months.

The vaccine meets the requirement of the immunogenicity guideline of the European Medicines Agency.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminum chloride hexahydrate, trisodium phosphate dodecahydrate, potassium chloride, thiomersal, disodium hydrogen phosphate dihydrate, potassium dihydrogen phosphate, sodium chloride and water for injection.

6.2 Incompatibilities

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

6.3 Shelf life

15 months.
The vaccine should be used immediately after opening.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C)
Do not freeze.
Store in the original package in order to protect from light.
For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

0.5 ml suspension in an ampoule (Type I glass) with a breaking point.

Pack size of 1: One ampoule and one sterile safety syringe with retractable needle in a box.

Pack size of 20: One box contains 20 ampoules.

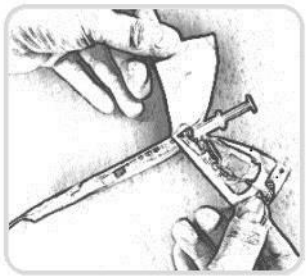
6.6 Special precautions for disposal and other handling

The vaccine should be allowed to reach room temperature before use.
Inspect intactness of the ampoule before opening.
Shake well before opening.
Check the homogeneity of the suspension after shaking.
Inhomogenous vaccines should not be used!

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

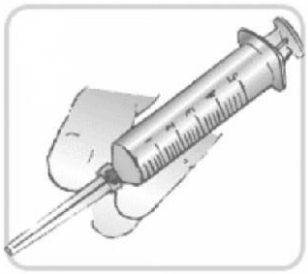
<u>The usage of the safety syringe – with retractable needle</u>
(Figures 1-6.)

(1)



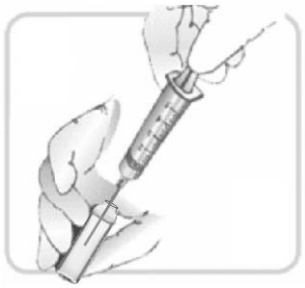
Open as shown above, but do not push the safety syringe plunger!

(2)



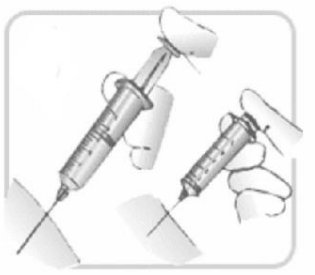
Remove the protective needle cover! Ensure that the plunger is not fully depressed beyond the first graduation mark of the safety syringe scale, otherwise the needle can only be retracted back into the barrel of the syringe and the syringe cannot be used.

(3)



Use standard technique to draw up medication. Ensure that the plunger is not fully depressed beyond the first graduation mark of the safety syringe scale.

(4)



Inject the medication by fully depressing the plunger.

(5)

Draw back plunger to retract the needle back to the barrel of the syringe.

(6)

Break off the plunger at the break point, and discard the complete unit into the hazardous-waste container. The needle cover and the broken parts of the plunger can be recycled.

Remark: ✠ (single cross)
Classification**: Group II**
Prescription-only medicine drug (POM)

7. MARKETING AUTHORIZATION HOLDER

Fluart Innovative Vaccines Ltd.
H-2097 Pilisborosjenő
Fő u. 7.

8. MARKETING AUTHORIZATION NUMBER(S)

OGYI-T-8998/03	1×0.5 ml	in glass ampoule
OGYI-T-8998/04	20×0.5 ml	in glass ampoule

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization: 9 June 2015

Date of latest renewal: -

10. DATE OF REVISION OF THE TEXT

September 2018