Registration No. 2C 20/45 (N)

Importer / Manufacturer: Biogenetech Co., Ltd. / Bellaria-Rosia-Sovicille (SI), Italy

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICAL PRODUCT
   FLUAD

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
   One dose (0.5 ml) contains:
   **Active Ingredients:** Influenza virus surface antigens (haemagglutinin and neuraminidase), propagated in fertilized hen’s egg from healthy chicken flocks and adjuvanted with MF59C.1, of strains:
   - A/California/07/2009 (H1N1) pdm09 – like strain
   - A/Texas/50/2012 (H3N2) – like strain
   - B/Massachusetts/2/2012 – like strain
   - A/California/07/2009, NYMC X-181
   - A/Texas/50/2012, NYMC X-223
   - B/Massachusetts/2/2012, wild type
   *haemagglutinin

   **Adjuvant:** MF59C.1 which is an exclusive adjuvant (Patent EP 0 399 843 B1): 9.75 mg squalene, 1.175 mg polysorbate 80, 1.175 mg sorbitan trioleate, 0.66 mg sodium citrate, 0.04 mg citric acid, and water for injections.

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

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

   Fluid may contain traces of eggs such as ovalbumin or chicken proteins, kanamycin and neomycin sulphate, formaldehyde, cetyltrimethylammonium bromide (CTAB) and barium phosphate which are used during the manufacturing process.

3. PHARMACEUTICAL FORM
   Suspension for injection in pre-filled syringe

4. CLINICAL PARTICULARS

   4.1 Therapeutic indications
   Active immunisation against influenza in the elderly (65 years of age and over), especially for those with an increased risk of associated complications (i.e. patients affected by underlying chronic diseases including diabetes, cardiovascular and respiratory diseases).

   4.2 Posology and method of administration
   A single 0.5 ml dose should be administered by intramuscular injection into the deltoid muscle.

   4.3 Contraindication
   Hypersensitivity to the active substances, components of the adjuvant excipient residues (e.g. egg or chicken proteins, such as ovalbumin) or in anyone who has had an anaphylactoid reaction to previous influenza vaccine.
The vaccine may contain residues of the following substances: kanamycin sulphate, neomycin sulphate, formaldehyde, cetyltrimethylammonium bromide (CTAB) and barium phosphate.

Immunisation shall be postponed in patients with febrile illness or acute infection.

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.

FLUAD should under no circumstances be administered intravascularly or subcutaneously.

Anxiety-related reactions, including vasovagal reaction (syncope), hyperventilation or stress-related reactions, 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 (due to illness) or iatrogenic (due to medicine) immunosuppression may be insufficient.

A protective response may not be elicited in all vaccinees.

4.5 Interaction with other medical products and forms of interaction
No clinical data on concomitant administration with other vaccines are available.
If FLUAD needs to be used at the same time as another vaccine, Immunisation should be carried out on separate limbs. It should be noted that the adverse reactions may be intensifies.
A higher frequency of some solicited systemic reactions has been reported in subjects vaccinated with trivalent inactivated influenza vaccine and pneumococcal compared with trivalent inactivated influenza vaccine alone.
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 results. The transient false positive reactions could be due to the IgM response by the vaccine.

4.6 Pregnancy and lactation
N/A

4.7 Effects on the ability to drive and use machines
FLUAD has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects
Like all medicines FLUAD can have side effects.
A higher incidence of mild post-immunisation reactions has been reported with FLUAD compared to non-adjuvanted influenza vaccines.

Adverse reactions observed from clinical trials.
The following undesirable effects have been observed during clinical trials with the following frequencies:

Very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000, <1/1,000); very rare (< 1/10,000), including isolated reports.

Nervous system disorders
Very common (≥1/10): Headache

Gastrointestinal disorders
Common (≥1/100, <1/10): Nausea, Diarrhoea, Vomiting

Skin and subcutaneous tissue disorders
Common (≥1/100, <1/10): Sweating
Uncommon (≥1/1,000, <1/100): Rash

Musculoskeletal and connective tissue disorders
Very common (≥1/10): Myalgia (muscular pain)
Common (≥1/100, <1/10): arthralgia (joint pain)

General disorders and administration site conditions
Very common (≥1/10): Tenderness, pain at injection site, fatigue
Common (≥1/100, <1/10): Fever, malaise (generally feeling unwell), shivering
Local reactions: redness, swelling, ecchymosis (bruising), induration (hardness)
Most reactions are mild or moderate and resolve spontaneously within 1-2 days.

Adverse reactions reported from post-marketing surveillance
Adverse reactions reported from post marketing surveillance are, next to the reactions which have also been observed during the clinical trials, the following:

Blood and lymphatic system disorders:
Thrombocytopenia (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, some very rare cases were severe with platelet counts less than 5,000 per mm$^3$), lymphadenopathy (swelling of the glands in the neck, armpit or groin).

General disorders and administration site conditions:
Asthenia, Influenza-Like Illness (ILI)
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, in rare cases leading to shock (medical emergency with a failure of the circulatory system to maintain adequate blood flow to the different organs), anaphylaxis and angioedema (swelling most apparent in the head and neck, including the face, lips, tongue, throat or any other part of the body).

Musculoskeletal and connective tissue disorders
Pain in the extremity, muscular weakness

Nervous system disorders:
Neurological disorders, such as encephalomyelitis, neuritis and Guillain-Barré syndrome (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), convulsions (fits), neuritis, neuralgia (pain situated on the nerve route), paraesthesia (abnormal feeling like burning, numbness, stinging, etc.), syncope (fainting) and presyncope (feeling faint)

Skin and subcutaneous tissue disorders:
Generalised skin reactions including erythema multiforme (severe skin rash), urticaria (hives), pruritus (itching) or non-specific rash.

Vascular disorders:
Vasculitis with transient renal involvement (blood vessel inflammation which may result in skin rashes and in very rare cases in temporary kidney problems)

If these reactions appear, consult a physician.

It is important to inform a physician of the appearance of any undesirable effects not described on this leaflet.

4.9 Overdose
N/A

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Seroprotection is generally obtained within 2 to 3 weeks. The duration of postvaccination immunity to homologous strains or to strains closely related to the vaccine strains varies, but it is usually 6-12 months. Although comparative field efficacy trials have not been performed, the antibody response to FLUAD is increased when compared to the response to vaccines without adjuvant, and is most pronounced for B and A/H3N2 influenza antigens. This increased response is seen particularly in elderly subjects with low pre-immunisation titre and/or with underlying diseases (diabetes and cardiovascular and respiratory diseases) who are at increased risk of complications of influenza infection. A similar immunogenicity profile has been noted after a second and third immunisation with FLUAD. Significant antibody rises after immunisation with FLUAD have also been shown against heterovariant strains, antigenically different from those included in the vaccine.

5.2 Pharmacokinetic properties
N/A

5.3 Preclinical safety data
N/A

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Sodium chloride, potassium chloride, potassium dihydrogen phosphate, disodium phosphate dihydrate, magnesium chloride hexahydrate, calcium chloride dihydrate, and water for injections.

6.2 Incompatibilities
N/A

6.3 Shelf life
1 year

6.4 Special precautions for storage
In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products. Any unused product or waste material should be disposed of in accordance with local requirements. Do not use the product after the expiry date indicated on the box after EXP. The expiry date refers to the last day of that month. Information regarding the medicinal product should always be kept at hand, therefore keep both the box and the package leaflet.

Store FLUAD in a refrigerator (2°C - 8°C). Do not freeze. Protect from light.

Keep medicines out of the reach and sight of children.

Medicinal product subject to medical prescription.

6.5 Nature and contents of container
1 Pre-filled syringe of one dose (0.5 ml).

6.6 Special precautions for disposal and other handling
N/A

7. MARKETING AUTHORISATION HOLDER
Biogenetech Co., Ltd.
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8. MARKETING AUTHORISATION NUMBER(S)
2C 20/45 (N)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
May 20, 2005

10. DATE OF REVISION OF THE TEXT
October 28, 2016