FLU-M®
[INFLUENZA VACCINE (SPLIT VIRION, INACTIVATED)]

1. NAME OF THE MEDICINAL PRODUCT

FLU-M® [Influenza vaccine (split virion, inactivated)].
Inactivated influenza vaccine.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

FLU-M® [Influenza vaccine (split virion, inactivated)] is a mixture of highly purified protective surface and internal antigens of influenza viruses of type A (H1N1, H3N2) and type B in a phosphate buffer solution. Influenza viruses are cultured in chicken embryos and inactivated by beta-propiolactone.

One dose of 0.5 mL contains:

Active ingredients:

IVR-215 A/Victoria/2570/2019 (H1N1)pdm09 – like virus	15 µg HA
IIVR-208 A/Hong Kong/2671/2019 (H3N2) – like virus	15 µg HA
B/Washington/02/2019 (B/Victoria linage)	15 µg HA

Excipients:

Thiomersal	50 µg
Triton X-100	not more than100 µg
Phosphate buffer solution (sodium chloride; disodium phosphate dodecahydrate; potassium dihydrogen phosphate; water for injections)	up to 0.5 mL

This vaccine complies with the WHO recommendations to strains for the Southern Hemisphere in the 2021 season.

3. PHARMACEUTICAL FORM

Solution for intramuscular injection in a multi-dose vial.
The vaccine is a slightly opalescent colorless liquid.

4. CLINICAL PARTICULARS

4.1 Pharmacological effect

The vaccine stimulates the production of serum antibodies against haemagglutinins of influenza virus and development of specific immunity to relevant strains of influenza type A and B. The duration of post-vaccination immunity to homologous strains or strains closely related to vaccine strains may vary, however, in most cases it is 6-12 months.

4.2 Therapeutic indications

FLU-M® [Influenza vaccine (split virion, inactivated)] is indicated for the prophylaxis of influenza caused by the seasonal viruses included in the vaccine.

The vaccine is indicated in people aged 6 years and older.

The vaccination should be carried out annually. Vaccination may also be carried out in periods when the incidence of influenza increases.

4.3 Posology and method of administration

The vaccine is administered in a single dose of 0.5 mL intramuscularly (into the deltoid muscle).

4.4 Contraindications

Vaccination should not be performed in the following conditions:
• History of severe allergic reactions to the use of influenza vaccines.
• History of severe allergic reactions to chicken protein and other vaccine components.
• Acute febrile states or aggravation of a chronic disease.
• Pregnancy and lactation.
• In case of not severe acute respiratory viral infections (ARVI) and acute intestinal diseases, vaccination is carried out after recovery (remission) of the disease.

4.5 Special warnings and precautions for use

The medical personnel responsible for the vaccination should measure the body temperature of all people to be vaccinated before using the vaccine, since it is not allowed to carry out vaccination in people with a body temperature higher than 37 °C.

Consultation and vaccination centers, where vaccination is carried out, must have all the necessary equipment and medicines required for the treatment of any adverse reactions that may develop after vaccination. All vaccinees should be under medical supervision for 30 minutes after injection of the vaccine.

Before use, the vaccine should be taken from the refrigerator and left until it reaches room temperature, the contents of the vial should be shaken. The vial cap should be treated with a disinfectant solution. The vial should be opened by removing an aluminum seal with plastic cap. Do not open the rubber stopper! Before taking each dose, the outer surface of the vial stopper should be treated with a disinfectant solution.

The extraction of each dose is done with a sterile disposable syringe and needle. A new syringe and needle should be used for each extraction. Disinfect the injection site. Immediately administer the prepared vaccine to a patient. In the intervals between dose extractions and not later than 5 minutes after the last dose extraction, the vial should be placed in the refrigerator (not in the freezer) for storage at a temperature of 2 to 8 °C. The vaccine from open multi-dose vials, after taking the first dose, must be used for subsequent immunization sessions within 28 days, provided that all use and storage requirements are met.
Pharmaceutical products should not be disposed of into sewers or together with household waste. Place vials from used medicinal products into containers for biological waste located in vaccination facilities for subsequent disinfection and processing by chemical or physical methods. If you have any doubts about the method of disposal of medicine waste and containers, please, contact a specialist. This will help protect the environment.

It is forbidden to use the vaccine in vials with evidence of violation of integrity (container closure system) or in case of changes in physical properties (color, transparency, appearance of particles, precipitates), expiration of the vaccine and violation of the cold chain or storage conditions.

The vaccine should be visually inspected prior to administration.

The vaccine is only intended to be administered intramuscularly.

4.6 Interaction with other medicines and other forms of interaction

The vaccine can be used simultaneously (on the same day) with other inactivated and live vaccines of the National Vaccination Schedule (except for rabies vaccines). In this case, the vaccines should be administered at different parts of the body (different limbs) using different syringes and needles. The vaccine should not be mixed with any pharmaceutical products, including vaccines, in the same syringe. The efficiency of vaccination can be adversely affected by an immunosuppressive therapy taken by the patient.
After influenza vaccination, an enzyme linked immunosorbent assay (ELISA) for HIV-1, hepatitis C virus and especially human T-cell lymphotropic virus type 1 (HTLV-1) can give false-positive serological test results. These transient false-positive results can be caused by the production of cross-reacting IgM antibodies in response to the vaccine.
Therefore, in order to confirm the diagnosis of HIV-1, hepatitis C virus or human T-cell lymphotropic virus (HTLV-1), it is necessary to obtain a positive result of a confirming virus-specific test (e.g., the Western blot method or immunoblot).

4.7 Incompatibilities

There is no data of compatibility studies.

4.8 Pregnancy and lactation

No data available, no clinical trials have been conducted.

4.9 Effect on the ability to drive and use machines

Trials of the effect of the drug on driving vehicles or machinery have not been conducted.

4.10 Adverse reactions

The frequency of side reactions reported in clinical trials is presented in accordance with the WHO classification of ADRs.
The frequency was determined according to the following criteria: very common (≥ 1/10), common (≥ 1/100 and <1/10), uncommon (≥ 1/1000 and <1/100), rare (≥ 1/10000 and <1/1000), very rare (<1/10000, including sporadic cases).

Tabla 1. Adverse reactions observed in clinical trials in persons in the 18-60 age group.

Adverse reactions according to the classes of organ systems according to medical dictionary for MedDRA regulatory activities	Frequency
Respiratory, thoracic and mediastinal disorders:	
Cough Sore throat	rare
Gastrointestinal disorders:	
Nausea	rare
General disorders and administration site conditions:	
Pain at the injection site Hyperemia at the injection site	common
Increased body temperature >37°C	uncommon
Chills	rare

The above adverse reactions develop on the day of vaccination, usually resolve spontaneously within 1-3 days and do not require any treatment. The medical personnel conducting the vaccination should draw the patient's attention to the fact that if any of the adverse reactions indicated in the instructions are aggravated or any other side effects not specified in the instructions occur the doctor must be informed.

Paediatric population

During the clinical trials, the safety of use of FLU-M® was assessed in 300 children aged 6 to 17 years. During the trial, no fundamental differences were found in the vaccine safety profile in the paediatric population as compared to the adult volunteers, all reactions were successfully resolved, and no severe or serious adverse reactions were recorded. In the age group of 6 to 11 years old, adverse reactions at

the injection site were slightly more frequent as compared to the group of 12–17 years old. Table 2 shows all adverse reactions recorded during the clinical trial.

Table 2. Adverse reactions observed in clinical trials in children of the 6 – 17 age group.

Adverse reactions according to the classes of organ systems according to medical dictionary for MedDRA regulatory activities	**Frequency**
General disorders and administration site conditions:	
Pain at the injection site* Hyperemia at the injection site	common
Increased body temperature >37 °C* Induration at the site of the injection Edema at the injection site*	uncommon
* the reactions were observed in the age group of 6 to 11 years old only	

Elderly patients
During the clinical trials, the safety of use of FLU-M® was assessed in 160 volunteers aged above 60 years. During the trial, the vaccine was well tolerated, all reactions were successfully resolved, no severe or serious adverse reactions were reported. In comparison with the age group of 18 to 60 years old, persons aged above 60 years additionally had such adverse events as headache and an increase in the serum IgE level without any clinical manifestations. Table 3 shows all adverse reactions recorded during the clinical trial.

Table 3. Adverse reactions observed in clinical trials in persons above 60 years old.

Adverse reactions according to the classes of organ systems according to medical dictionary for MedDRA regulatory activities	**Frequency**
Nervous system disorders:	
Headache	uncommon
General disorders and administration site conditions:	
Hyperemia at the injection site	common
Laboratory and instrumental data:	
Increasing of immunoglobulin E (IgE) in blood	very common

Description of individual adverse events.
An increase in the level of immunoglobulin E in the population over 60 years old during the clinical trial was recorded in 27.5 % of volunteers, however, in all cases the IgE level was slightly increased and was not accompanied by allergic reactions.

4.11 Overdose
No cases of overdose have been reported.

5. PHARMACOTHERAPEUTIC GROUP
Viral vaccines, ATC code: J07BB02

6. NATURE AND CONTENTS OF THE PACKAGE
10 multi-dose vials of 5 mL (10 doses of 0.5 mL each) of FLU-M® [Influenza vaccine (split virion, inactivated)], with a package leaflet.

7. SPECIAL STORAGE PRECAUTIONS
The vaccine must be stored in refrigerator at 2 °C to 8 °C. Do not freeze. Keep out of the reach of children. Store the vial in the external package to protect it from light.

8. TRANSPORTATION CONDITIONS
Transport at a temperature of 2 °C to 8 °C. **Do not freeze.**
It is allowed to transport at a temperature of up to 25 °C for not longer than 6 hours.

9. SHELF LIFE
Unopened vial
One year (12 months) from the date of manufacture.
Opened vial
Opened multi-dose vials can be kept and used in subsequent immunization sessions for up to 28 days after first opening, provided that the following conditions are met: 1) the vaccine vial has been stored and will continue to be stored at 2-8°C, 2) the expiry date of the vaccine has not passed.
Do not use an expired product.

10. SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING
Any open multi-dose vial should be discarded 28 days after the first use. An individual sterile syringe and needle should be used for each injection to prevent the transmission of infectious agents from one individual to another. Needles should be disposed of properly and should not be reused.
Disposed of any unused vaccine in accordance with local regulations.

11. MANUFACTURER

MARKETING AUTHORIZATION HOLDER AND MANUFACTURER

Federal State Unitary Enterprise "Saint Petersburg Scientific Research Institute of Vaccines and Sera and Enterprise for the Production of Bacterial Preparations" of the Federal Medical and Biologic Agency (FSUE SPbSRIVS FMBA of Russia)
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FILLING AND PACKAGING

Instituto Latinoamericano de Biotecnología MECHNIKOV, S.A.
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Complaints about FLU-M® [Influenza vaccine (split virion, inactivated)] quality defects, as well as information about high reactogenicity or the development of medical complications associated with the use of the vaccine, should be submitted to FSUE SPbSRIVS FMBA of Russia and Instituto Latinoamericano de Biotecnología MECHNIKOV, S.A. with the indication of vaccine identification data specified on web-pages: www.spbniivs.ru and www.mechnikov.com

Marketing Authorization number in Cuba: B-20-080-J07

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