MINISTRY OF HEALTH OF THE RUSSIAN FEDERATION

PACKAGE INSERT

FOR MEDICAL PRODUCT

Gam-COVID-Vac, combined vector vaccine for the prevention of coronaviral infection caused by the SARS-CoV-2 virus

▼ This drug is registered according registration procedure for drugs intended for use in the situation of a potential or actual emergency. This insert is prepared based on limited clinical data and will be complemented as new data becomes available. The drug can only be administered at healthcare institutions authorized to vaccinate the population as per the established procedure.

Marketing authorization number: LP-006395

Trade name: Gam-COVID-Vac combined vector vaccine to prevent SARS-CoV-2-induced coronavirus infection

International nonproprietary or generic or chemical name: Vaccine to help prevent the newly discovered coronavirus infection (COVID-19)
Presentation: solution for intramuscular injection

Composition per dose.
Component I contains:
Active substance: recombinant serotype 26 adenoviral particles, containing the SARS-CoV-2 protein S gene, in the amount of (1.0±0.5) x 10^{11} particles per dose. *Excipients:* tris-(hydroxymethyl)aminomethane - 1.21 mg, sodium chloride - 2.19 mg, sucrose - 25.0 mg, magnesium chloride hexahydrate - 102.0 μg, EDTA-disodium salt dihydrate – 19.0 μg, polysorbate 80 - 250 μg, ethanol 95% - 2.5 μL, water for injections up to 0.5 mL.
Component II contains:
Active substance: recombinant serotype 5 adenoviral particles, containing the SARS-CoV-2 protein S gene, in the amount of (1.0±0.5) x 10^{11} particles per dose. *Excipients:* tris-(hydroxymethyl)aminomethane - 1.21 mg, sodium chloride - 2.19 mg, sucrose - 25.0 mg, magnesium chloride hexahydrate - 102.0 μg, EDTA-disodium salt dihydrate – 19.0 μg, polysorbate 80 - 250 μg, ethanol 95% - 2.5 μL, water for injections up to 0.5 mL.

Description:
Component I. Frozen solution. It is a dense, solidified mass whitish in color. After thawing: a homogeneous solution, colorless or with a yellowish hue, slightly opalescent.
Component II. Frozen solution. It is a dense, solidified mass whitish in color. After thawing: a homogeneous solution, colorless or with a yellowish hue, slightly opalescent.

Description: The vaccine is produced using biotechnology, without using the SARS-CoV-2 virus pathogenic for humans. The drug contains two components: Component I and Component II. Component I includes a recombinant adenoviral vector that uses a serotype 26 human adenovirus carrying a SARS-CoV-2 protein S gene. Component II includes a serotype 5 human adenoviral vector carrying a SARS-CoV-2 protein S gene.

version 28.12.2020 (LP-006395-110820, with amend. 1,3,5,6)

Pharmacotherapeutic group: medical immunobiological vaccine.

ATC code: J07B

Pharmacological properties
The vaccine induces the formation of humoral and cellular immunity to the coronavirus infection caused by the SARS-CoV-2 virus.
Immunological efficacy
The immunological properties and safety of the vaccine have been studied in various clinical trials in adult volunteers of both sexes over the age of 18. An intermediate immunogenicity review revealed that the vaccine had formed an immune response in the subjects. A humoral immune response study serum samples taken from volunteers were analyzed for antibodies specific to the SARS-CoV-2 S glycoprotein receptor-binding domain on the 42nd day from the start of vaccination: in the treatment group had an antibody geometric mean titer of 8996; and seroconversion level of 98.25%. When comparing RBD-specific antibody levels among age strata a statistically significant difference was demonstrated for the 18-30 years group relative to the other groups: antibody geometric mean titer was 18102-22067, seroconversion level - 100%. There was no statistically significant difference between males and females in antibody levels. On the 42nd day from the start of vaccination neutralizing antibody geometric mean titer in inoculated volunteers was 44.47, seroconversion level - 95.83%. No statistically significant difference was revealed among volunteers of different sex or age.
Immunization with the drug Gam-COVID-Vac has formed expressed antigen-specific, cell-mediated anti-infection immunity in practically 100% of the volunteers (the formation of antigen-specific cells for both populations of T lymphocytes: T helpers (CD4+) and T killers (CD8+), along with a statistically significant increase in the secretion of IFN-gamma).
The protective antibody titer is currently unknown. The duration of protection is unknown.
Clinical epidemiological efficacy studies are ongoing. According to an interim analysis, the efficacy is over 91%.

Indications for use:
Teh prevention of the newly discovered coronavirus infection (COVID-19) in adults over the age of 18.

Contraindications:
- Hypersensitivity to any of the vaccine components, or a vaccine containing similar components;
- severe allergic reactions in the past;
- acute infectious and non-infectious diseases, flares of chronic diseases - vaccination is to be administered 2-4 weeks after recovery or remission. In non-severe ARVI or acute gastrointestinal infections - vaccination is administered after the body temperature normalizes;
- pregnancy and breastfeeding;
- age under 18 (due to lack of data on safety and efficacy)

Contraindications for component II
- severe post-vaccination complications (anaphylactic shock, severe generalized allergic reactions, convulsive disorder, temperature above 40°C, etc.) after administering the vaccine Component I.

Use with Caution
Using with caution: the vaccine should be used with caution in cases of chronic liver and kidney disease, endocrine disorders (apparent thyroid function abnormalities and diabetes mellitus in decompensation stage), serious diseases of the hematopoietic system, epilepsy and other CNS diseases, acute coronary syndrome and acute cerebrovascular event, myocarditis, endocarditis,

pericarditis.
Due to lack of data, vaccination may be a risk for the following groups of patients:

- with autoimmune diseases (stimulation of the immune system can lead to an exacerbation of the disease, special caution should be exercised with patients with an autoimmune disorder that tend to lead to severe and life-threatening conditions).
- with malignant neoplasms

The decision to vaccinate should be based on the assessment of a benefit/risk ratio in each specific situation.

The sites of vaccination must have anti-shock treatment in place (as per Directive No. 1079n of the Ministry of Health of the Russian Federation of December 20th, 2012 "On the endorsement of standard emergency care in the case of an anaphylactic shock").
On the vaccination day, the volunteer must be examined by a doctor: a physical and taking body temperature are mandatory; if body temperature is above 37°C, the vaccination is not to be administered.

Use during pregnancy and while breastfeeding
The drug is contraindicated during pregnancy and breastfeeding, since its efficacy and safety for those periods have not been studied.

Administration route and dosage:
The vaccine is for intramuscular injection only. Intravenous administration of the drug is strictly prohibited. The vaccine is injected into the deltoid muscle (the upper third of the outer shoulder surface). If it is impossible to inject the drug into the deltoid muscle, the drug is injected into the vastus lateralis. The vaccination is administered in two stages: first 0.5 mL of Component I, and then, three weeks afterwards, 0.5 mL of component II is injected.
After administering the vaccine, the medical staff is to monitor the patient's state of health over a period of 30 minutes.
Preparing a solution for injection. Prior to vaccination, take a vial or ampoule with Component I or Component II out of the freezer and leave at room temperature till completely thawed. No ice inclusions are permitted. Clean the vial or ampoule of residual moisture with an alcohol wipe. Stir the contents carefully by rocking the container. No shaking of the vial or ampoule are allowed!
Remove the protective plastic overlay from the vial and treat the rubber stopper with an alcohol wipe.
With a single-use syringe, draw 0.5 mL of the drug as a dose to administer to a patient. If subsequent injections are postponed for some reason, an open 3.0 mL vial may be stored for at most 2 hours at room temperature. Storing an open 0.5 mL vial (ampoule) is not allowed!

Re-freezing of a vial with the drug is not allowed!
The drug kept in a vial or ampule with compromised integrity and/or labelling, of changed physical properties (opalescence, coloration), subjected to improper storage and/or with expired shelf life is unfit for use.

▼Information for healthcare workers carrying out vaccination with the drug: this medicinal product has been authorized through a special marketing authorization procedure, hence each use of the medicinal drug must be reported to the Federal Healthcare Oversight Agency by entering the information into the relevant section of the Uniform State Health Information System.

Side effects
Adverse reactions specific to the use of the vaccine, revealed in clinical trials and studies of other vaccines based on a similar technological platform, are predominantly of mild or medium severity, and may develop during the first or second day following vaccination and usually abate within 3

subsequent days. The most common include short-term general (a brief flu-like syndrome characterized by chills, fever, arthralgia, myalgia, asthenia, general discomfort, headache) or local (injection site tenderness, hyperemia, swelling) reactions. Non-steroidal anti-inflammatory drugs (NSAIDs) are recommended in case of post-vaccination fever and antihistamines for expressed local reactions.

Less common ones are nausea, dyspepsia, loss of appetite, occasionally - enlarged regional lymph nodes. Some volunteers may develop allergic reactions, short-term elevated liver transaminase levels, elevated serum creatinine and creatine phosphokinase levels.

Within the Gam-COVID-Vac safety, tolerability and immunogenicity clinical trials conducted to date the following AEs have been registered:

General injection site disorders and reactions: hyperthermia, vaccination site tenderness, edema and pruritus, asthenia, pain, malaise, pyrexia, increased vaccination site skin temperature, decreased appetite. Inicidence rate - very common and common.

Respiratory, chest, and mediastinal disorders: oropharyngeal pain, nasal congestion, sore throat, rhinorrhea. Incidence rate – common

Nervous system disorders: common – headache; rare –.dizziness, syncope

Gastrointestinal disorders: nausea, vomit, dyspepsia - common.

Lab test and instrumentation data: divergent deviations of immunological status indicators: increased count of T-lymphocytes, increase in the percentage of lymphocytes, decreased count of natural killer cells, increased count of CD4-lymphocytes, decreased count of CD4-lymphocytes, increased count of B-lymphocytes, decreased count of B-lymphocytes, increased count of natural killer cells, increased count of CD8 lymphocytes, increased level of immunoglobulin E (IgE) in the blood, increase in the CD4/CD8 ratio, decrease in the CD4/CD8 ratio, increased level of immunoglobulin A (IgA) in the blood, decrease in the percentage of CD8 lymphocytes. Abnormalities in the complete blood count: increase in the percentage of lymphocytes, decrease in the hematocrit, increased count of lymphocytes, increase in the erythrocyte sedimentation rate, increased leukocyte count, increased count of monocytes, increased platelet count, decreased count of neutrophils, decreased platelet count. Deviations in common urine analysis: erythrocytes in the urine.

Most AEs ended in complete abatement, without any consequences. Lab test deviations were not of clinical significance (did not require additional diagnostics or therapy).

Overdosage

So far no cases of overdosage have been reported.

Since the drug is supposed to be used only at healthcare centers, and vaccination is to be carried out by qualified medical staff only, the risk of overdosing is extremely low.

However, it may be safely assumed that in case of inadvertent overdosage a patient may develop more severe forms of the above toxic and toxicoallergic reactions. No specific antidote to the drug exists.

Therapeutic intervention in this case will include symptomatic treatment based on indications (antipyretics/ NSAIDs and antisensitizers), corticosteroids parenterally in case of an expressed toxicoallergic syndrome). The administration schedule should be based on the recommendations for the use and dosing of the respective drugs.

Drug-to-drug interactions

Has not been studied.

Specific Instructions

Patients receiving immunosuppressive therapy and immunodeficient patients may not develop sufficient immune response. Therefore, any drugs that suppress the immune system’s function are contraindicated within at least 1 month before and after vaccination due to the risk of immunogenicity reduction.

Influence on the ability to drive and use machines No studies on the effects on the ability to drive and use machines have been conducted.

Presentation
Solution for intramuscular injection, Component I - 0.5 mL/dose + Component II - 0.5 mL/dose.
When manufactured by FSBI N.F. Gamaleya NRCEM of the Ministry of Health of Russia (Medgamal Branch of FSBI N.F. Gamaleya NRCEM of the Ministry of Health of Russia): 0.5 mL (1 dose) of each drug component in a hydrolytic class I neutral glass vials (2R, 4R type) hermetically closed with rubber stoppers and aluminum or aluminoplastic crimp caps.
Vials are labeled with a writing paper or label paper label or adhesive one.
A Component I vial with a package insert is placed in a carton or cardboard pack; a Component II vial with a package insert is placed in a carton or cardboard pack.
When manufactured by JSC Binnopharm: 0.5 mL (1 dose) of each drug component is in hydrolytic class 1 colorless glass color-coded 1 mL ampoules. A label is attached to each ampoule.
5 ampules of each drug component are packed in a PVC blister pack.
1 blister pack with the product instructions is placed into a pack made from cardboard.
When manufactured by JSC GENERIUM:
3.0 mL (5 doses) of each component are placed in neutral glass vials of hydrolytic class 1, format 2R; hermetically closed with rubber stoppers and aluminoplastic tamper-proof crimp caps.
An adhesive label is attached to each drug component vial.
A component I or component II vial with a package insert is placed in a cardboard pack or from imported cardboard with an elastic polyurethane foam holder.
When manufactured by CJSC BIOCAD:
0.5 mL of each component of the product in hydrolytic class I neutral glass vials (type 2R, 6R), hermetically sealed with a rubber stopper, aluminum crimp cap and a flip-off plastic top.
An adhesive label is attached to vials with each drug component.
A 6R vial with Component I or Component II with a package insert is placed in a carton.
A 2R vial with Component I or Component II in a PVC blister with a package insert is placed in a carton.

Storage: Store in a dark place at a temperature not exceeding minus 18°C.
Storing a thawed product in 0.5 mL vials (ampoules) is not allowed!
The thawed drug can be stored in 3.0 mL for 2 hours at most.
Re-freezing is not allowed.
Keep out of the reach of children.

Transportation: Transport the drug at a temperature not exceeding minus 18°C.

Shelf life: 6 months. Do not use beyond the shelf life.

Prescription status: for treatment and prevention institutions.

Manufacturer
Names and addresses of production sites of the drug manufacturer:
1) FSBI N. F. Gamaleya National Research Center of Epidemiology and Microbiology, Ministry of Health of the Russian Federation (Medgamal Branch of FSBI N.F. Gamaleya NRCEM of the Ministry of Health of Russia), Russia, 123098, Moscow, ul. Gamalei, 18 (all production stages).
2) JSC Binnopharm, Russia, 124460, Moscow, Zelenograd, ul. Konstruktora Guskova, 3, bld. 1 (cleaning, filling (primary package), packaging (secondary (consumer) package).
3) JSC GENERIUM, Russia, 601125, Vladimir Region, Petushki District, Volginsky settlement, Zavodskaya str, bld. 263 (finished dosage form manufacturing, primary and secondary (consumer)

packaging).
4) CJSC BIOCAD, Russia, 198515, Saint Petersburg, Strelna, ul. Svyazi, 38, bld. 1 (finished dosage form manufacturing, primary and secondary (consumer) packaging).

Release quality control
Medgamal Branch of FSBI N. F. Gamaleya National Research Center of Epidemiology and Microbiology, Ministry of Health of the Russian Federation. Russia,
123098 Moscow, Gamaleya Street, 18

Marketing authorization holder/claims management company:
Federal Government Budgetary Institution N. F. Gamaleya National Research Center of Epidemiology and Microbiology of the Ministry of Health of the Russian Federation (FSBI N.F. Gamaleya NRCEM of the Ministry of Health of Russia).
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Director
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/round stamp/

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