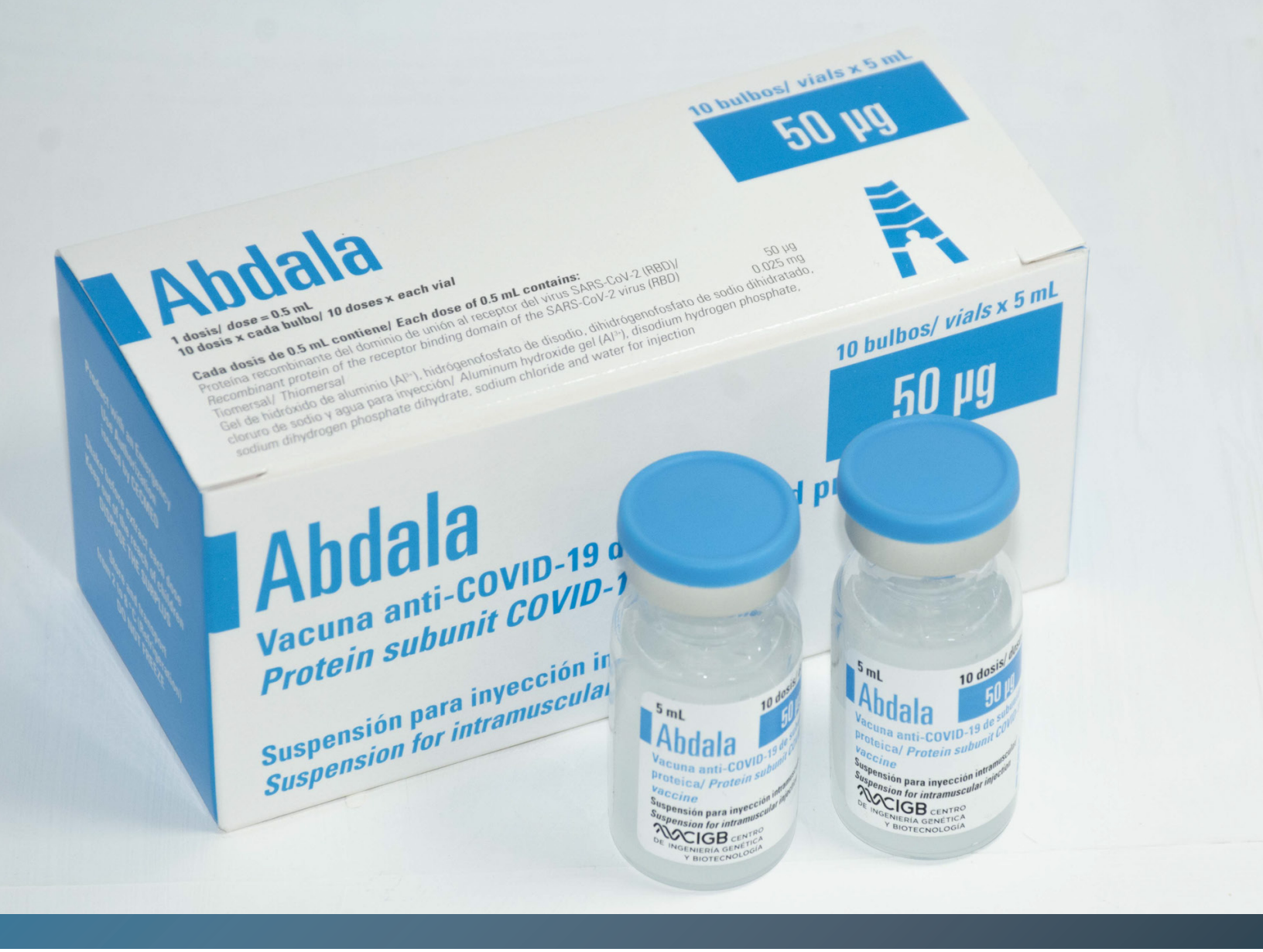

Abdala

PRODUCT WITH EMERGENCY USE AUTHORIZATION ISSUED BY CECMED

Emergency Use Authorization No.: Resolution No. 113/21.
Authorization issue date: July 9, 2021

CURRENT STATUS

Authorization for Emergency Use in Cuba and Venezuela

Phase I/II of clinical trial in convalescent COVID-19 (phase I concluded):
https://rpcec.sld.cu/ensayos/RPCEC00000382-Sp

Phase I/II of clinical trial in pediatric ages (3-18 years of age):
https://rpcec.sld.cu/ensayos/RPCEC00000381-Sp

CIGB CENTRO DE INGENIERÍA GENÉTICA Y BIOTECNOLOGÍA

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Abdala

CHARACTERISTICS OF THE VACCINE

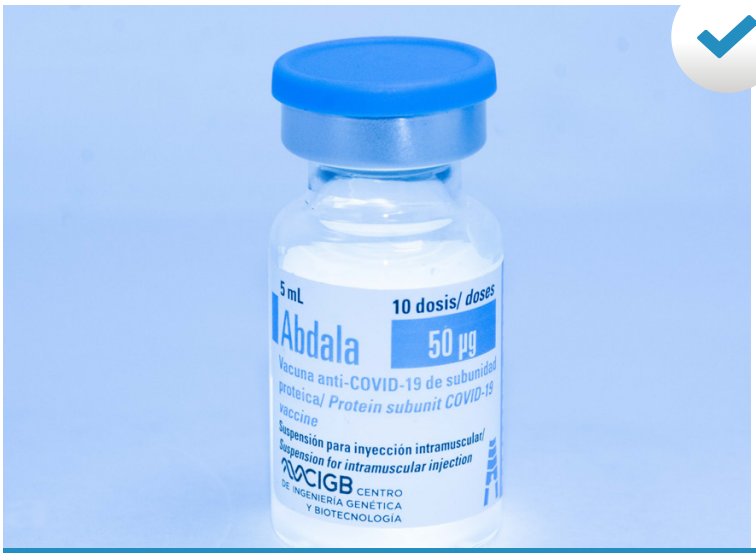
During the pandemic caused by the SARS-CoV-2 virus, it has been observed that most of the neutralizing antibodies and approximately 50% of the cellular response against this virus, are directed to the spike protein (S), which It contains the receptor-binding domain (RBD), which is the angiotensin-converting enzyme 2 (ACE2).

Abdala is a subunit vaccine, developed for vaccination against the SARS-CoV-2 virus. As active pharmaceutical ingredient it contains the receptor-binding domain (RBD) and as inactive ingredients it contains phosphate salts and aluminum hydroxide gel adjuvant.

It is manufactured in the Center for Genetic Engineering and Biotechnology (Havana, Cuba), with a production system of more than twenty years of experience, complying with current good production practices and in accordance with the recommendations of the World Health Organization (WHO).

Abdala is administered intramuscularly in a short schedule of three doses separated by 14-day intervals (in 0-14-28 days schedule). So far, this vaccine has been shown to be stable at a storage temperature between 2 and 8 °C.

Abdala's production platform is based on the yeast *Pichia pastoris*, which has been used by the CIGB in the Heberbiovac HB® preventive recombinant vaccine against the hepatitis B virus, which is registered in more than 30 countries and certified by the WHO.



CLINICAL RESULTS

Results from phase I/II clinical trials demonstrated that Abdala is a safe and well-tolerated vaccine. In phase I, 132 subjects were included, while in phase II, 660 volunteers were included. 403 adverse events of 56 different types were described. 80 % of these adverse events did not require medication during phase II. 97.8 % of adverse events were mild, and no serious adverse events were reported. 90 % of the subjects who received the Abdala vaccine 42 days after immunization seroconverted more than four times with respect to the initial time. And 72 % of the subjects inoculated with Abdala inhibited the binding of the SARS-CoV-2 virus to the ACE2 receptor by more than 30 %.

On March 22, 2021, the CIGB began the phase III clinical study, in which 48,290 subjects were included, of which 97 % completed the immunization schedule with the three doses.

Recently the efficacy result of 92.28 % of Abdala has been reported. On July 9, 2021, the Cuban regulatory authority Center for State Control of Medicines, Equipment and Medical Devices (CECMED) granted Abdala's Emergency Use Authorization.

Currently, progress is being made in the clinical trial of Abdala in pediatric ages between 3 and 18 years of age, as well as in the evaluation for the use of a booster dose in convalescent subjects of COVID-19.

92.28 % efficacy against symptomatic disease

100 % effective in preventing severe systemic disease

100 % efficacy in preventing death in vaccinated

The efficacy of Abdala, evaluated in phase III, was measured in a context where the alpha and beta strains of SARS-CoV-2 were circulating.

Abdala

ADVANTAGES

- Abdala is a vaccine based on the subunit protein, so there is no risk of pathogenicity, whose toxicity is very low, which ensures its high safety.
- The production system with which this vaccine is manufactured is robust.
- It is a potential vaccine that can protect against mutant strains from the use of booster doses without causing reactogenicity.
- The RBD antigen, designed by researchers at the CIGB, has peculiar characteristics that reinforce its immunogenic properties.

The Abdala vaccine is supported by intellectual property, which claims the design and production of chimeric antigens and their compositions, which generate a robust immune response when delivered by different routes of administration.

Patent number: CU 2020-0081,
filed Nov 4, 2020.

PUBLICATIONS

1. In-solution buffer-free digestion for the analysis of SARS-CoV-2 RBD proteins allows a full sequence coverage and detection of post-translational modifications in a single ESI-MS spectrum. Disponible en https://www.biorxiv.org/content/10.1101/2021.05.10.443404v1

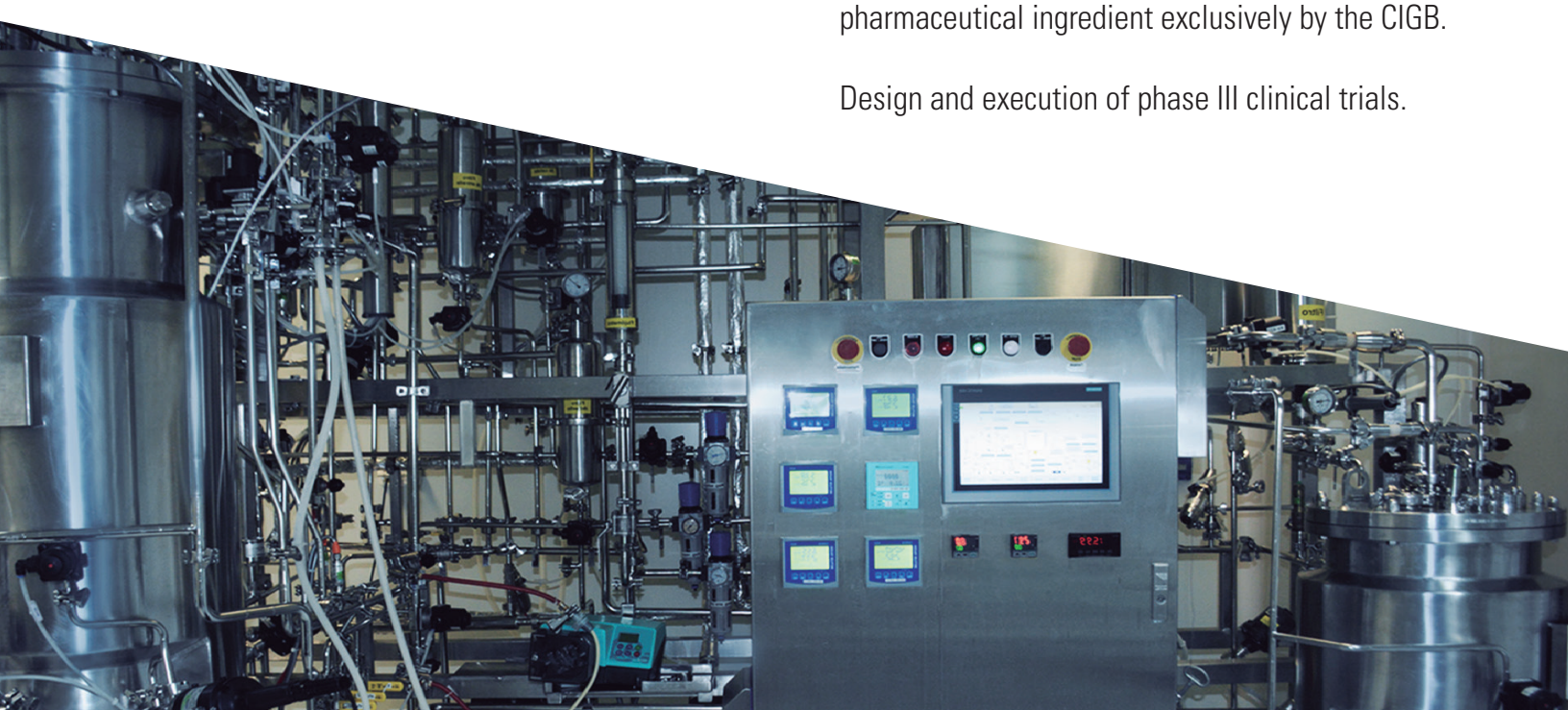
2. The SARS-CoV-2 receptor-binding domain expressed in *Pichia pastoris* as a candidate vaccine antigen. Disponible en https://www.medrxiv.org/content/10.1101/2021.06.29.21259605v1

The CIGB has extensive experience in the production and marketing of vaccines. For the Abdala vaccine there are alternatives such as:

Sale of vaccine (finished product) for marketing in authorized territories.

Technology transfer of the formulation, filling and packaging stages, including the sale of the active pharmaceutical ingredient exclusively by the CIGB.

Design and execution of phase III clinical trials.



PHARMACEUTICAL FORM
Suspension for injection

ROUTE OF ADMINISTRATION
Intramuscular injection

COMPOSITION
Each 0.5 mL dose contains:
Recombinant protein of the SARS-CoV-2 virus receptor-binding domain (RBD) 0.05 mg
Thiomersal 0.025 mg
Aluminum hydroxide gel
Disodium hydrogen phosphate
Sodium dihydrogen phosphate dihydrate
Sodium chloride
Water for injection, sq

STORAGE CONDITIONS
Abdala vaccine should be stored at 2-8 °C. Do not freeze. Discard vaccine if frozen.

PERIOD OF VALIDITY
6 months

EXPIRATION
The expiration date of the product kept in these conditions is indicated on the label and on the packaging.

THERAPEUTIC INDICATIONS
Abdala is indicated for specific active immunization in adults against SARS-CoV-2 virus infection.

CONTRAINDICATIONS
People under 19 years of age.
It should not be administered to people with known hypersensitivity to any of the components of the vaccine (including thiomersal).

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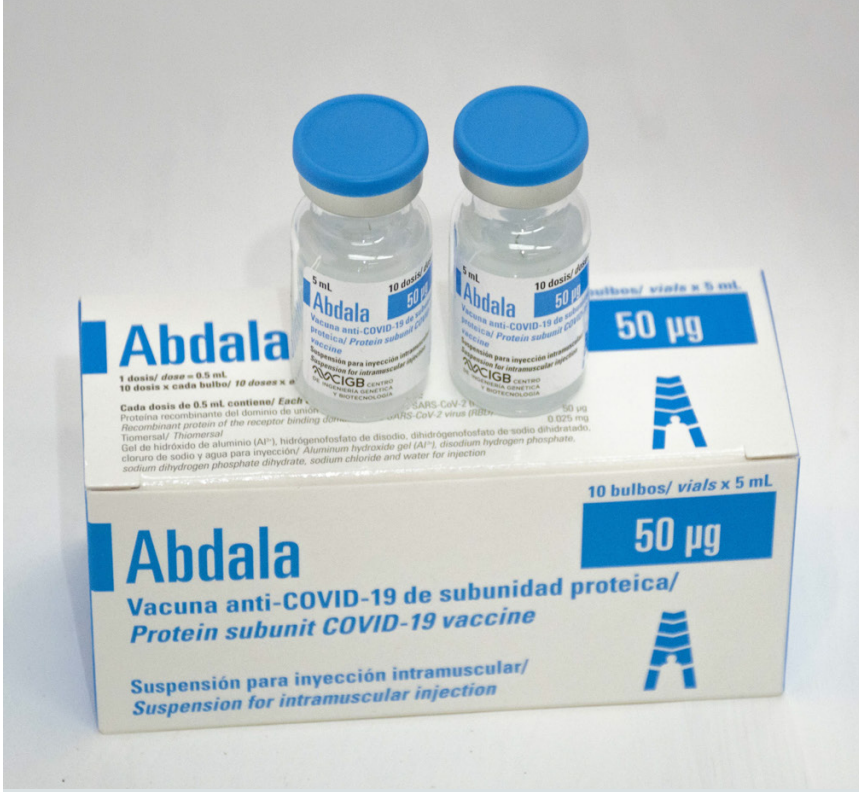


Abdala

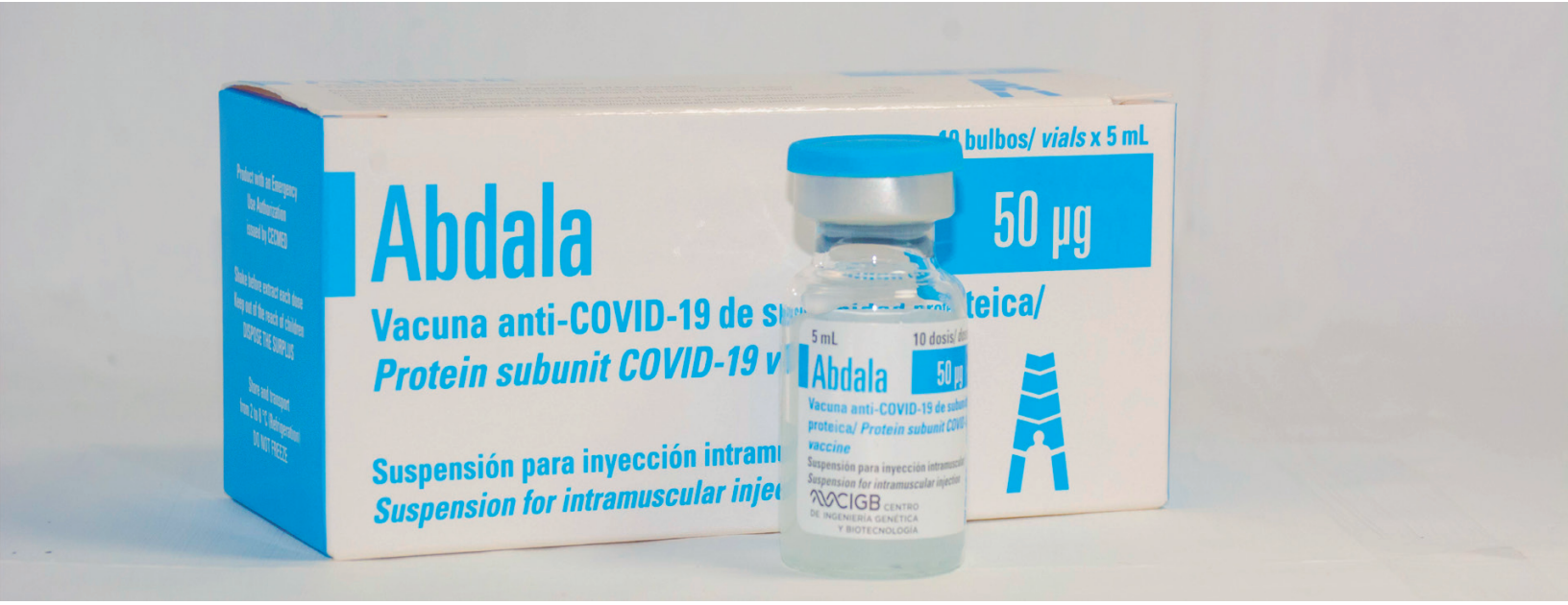
PRECAUTIONS

As with all vaccines, it is important to have an epinephrine hydrochloride solution (1:1000) available for immediate use in case of anaphylaxis or acute post-vaccination hypersensitivity reaction. For this reason, it is advisable to keep the individual under medical observation for 60 minutes after the administration of the vaccine. For people who have experienced anaphylaxis with the first dose of Abdala vaccine, a second dose should not be given.

People with chronic, autoimmune or endocrinometabolic diseases must be compensated at the time of vaccination. Taking vital signs is recommended prior to vaccination with Abdala. In case of arterial hypertension, it is suggested to defer immunization until blood pressure control is evident.

In individuals who report acute infection in the last 15 days, inoculation with Abdala should be deferred until resolution of the infection.

Convalescents from COVID-19 must follow the vaccination protocol approved for these cases.



SPECIAL WARNINGS AND PRECAUTIONS FOR USE

It is recommended to visually inspect the bulb before administration of Abdala. It is forbidden to use the bulb with evidence of violation of its physical integrity (of the container-closure system) or changes in the physical properties of the suspension (color, transparency, appearance of particles, precipitates).
Shake before extracting each dose.
It should not be administered by intravenous injection.

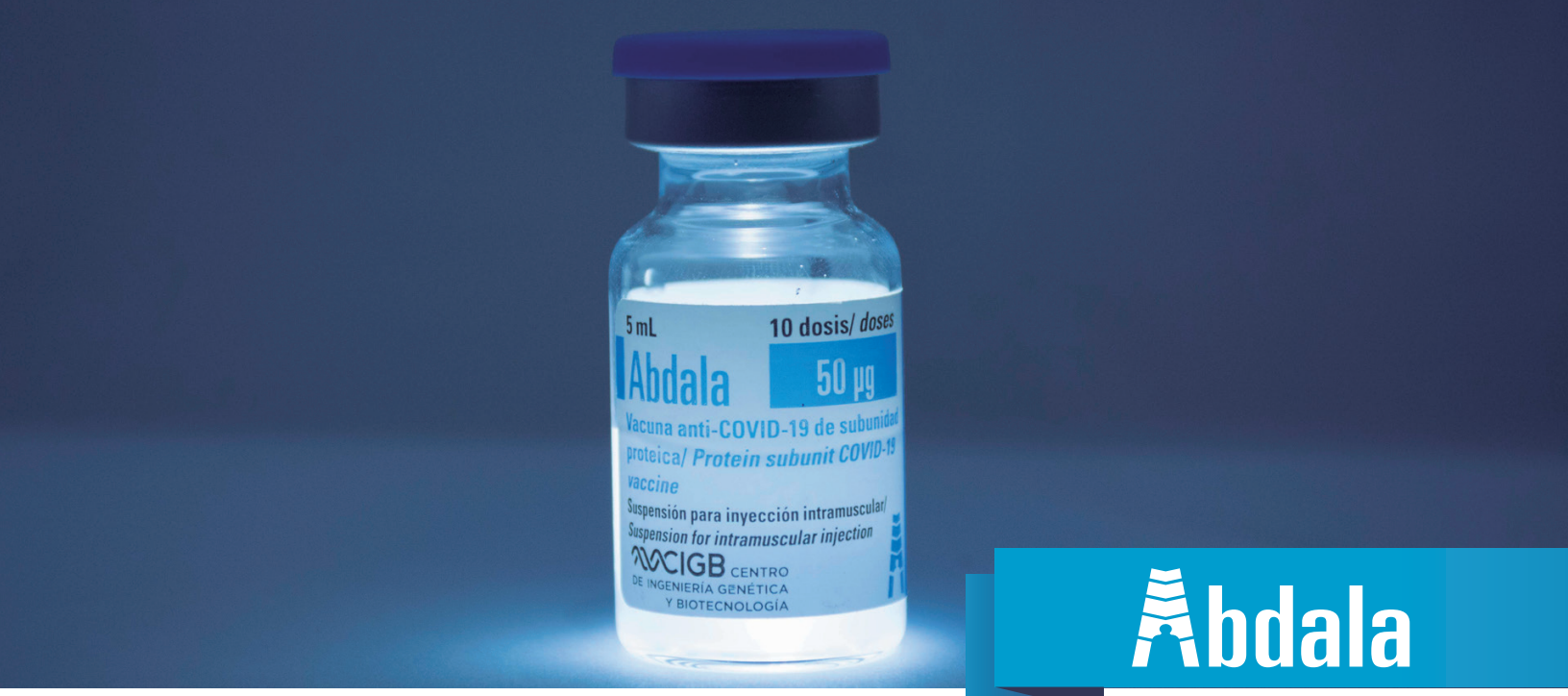
DOSAGE AND METHOD OF ADMINISTRATION

Dosage and administration schedule
A dose of 0.5 mL of Abdala vaccine should be administered.
It is applied with a three-dose schedule with an interval of 14 days between each dose.
Administration mode
Abdala is given by intramuscular injection in the deltoid region.
It should not be administered by intravenous injection.

UNDESIRABLE EFFECTS

Clinical experience shows that after the application of the Abdala vaccine in adults, most of the adverse events are mild (97 %), and resolve spontaneously without drug treatment, with a higher occurrence in the 24 to 48 hours after administration. of the vaccine.
The frequency of recording adverse events is higher after the application of the first dose of the vaccination schedule, and decreases after the application of subsequent doses.
After evaluating the safety after the application of 215 267 doses in the intervention clinical trial in risk cohorts, the safety profile evidenced in the clinical development of the product is confirmed.
The frequency of appearance of adverse reactions is low, between 0.1 and 1 % of the total doses applied, mainly local, with a predominance of pain, in addition to erythema and induration (0.85 %).
Systemic adverse reactions include headache (0.54 %), hypertension (0.27 %), somnolence (0.18 %), and asthenia (0.14 %).

Data continues to be collected to determine the causal relationship of arterial hypertension with the vaccine, since its appearance depends on multiple factors, and in clinical trials with the product, the frequency of this event has been similar to that observed in the control group (placebo).
Other adverse reactions have been described that occur with a frequency less than 0.1% of the applied doses, such as nausea, vomiting, arthralgia and general malaise.
After the application of more than 3 000 000 doses in the health intervention in populations and territories at risk, the appearance of anaphylaxis has been registered with a frequency of 0.19 per 100 000 applied doses, considered as a very rare adverse reaction (< 1/10 000).
No other serious adverse reactions have occurred. There are no deaths associated with vaccination with Abdala.



Abdala

INTERACTIONS WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

No information is available about the interaction of Abdala with other vaccines.
Immunosuppressive therapy can interfere with the response to the vaccine.

INSTRUCTIONS FOR USE, HANDLING AND DESTRUCTION OF THE UNUSABLE REMAINDER OF THE PRODUCT

Extreme hygienic-sanitary and biosafety measures during the inoculation of the vaccine and for the elimination of the materials used.

For each injection, use a sterile syringe and needle.

The bulbs used must be handled and destroyed in accordance with the instructions established in the vaccinations by the Ministry of Public Health of Cuba.

Multi-dose bulbs that have not been fully used in one immunization session cannot be kept for other sessions, and the remainder must be discarded at the end of the immunization day.

USE IN PREGNANCY AND LACTATION

Experience with the use of Abdala vaccine in pregnant women is limited. Animal studies do not suggest direct or indirect harmful effects with respect to pregnancy, embryo-fetal development, parturition or postnatal development. Administration of Abdala should only be considered during pregnancy, if the possible benefits outweigh the possible risks to the mother and fetus, based on medical judgment.
There is insufficient evidence to contraindicate the use of Abdala in breastfeeding women.

CIGB CENTRO DE INGENIERÍA GENÉTICA Y BIOTECNOLOGÍA

Distinctive company of Cuban biotechnology that develops, produces, markets and exports innovative products for the biomedical, veterinary, agricultural, aquaculture and industrial sectors, for a single health. It has a portfolio of research and development (R&D) projects and products, protected by patents. Its more than 30 products marketed in more than 35 countries, include vaccines, diagnostic tests, and first and only drugs of its kind, to treat diseases that do not have other effective therapeutic solutions. Several of its products are inserted in national programs to offer integral health care. It works with social responsibility and in harmony with the environment.

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