COVID-19 vaccine (MVC COVID-19 vaccine) is a drug, manufactured by Medigen Vaccine Biologics Corp., approved by the Ministry of Health and Welfare through the Emergency Use Authorization procedure, and is not subject to regular approval procedures. This vaccine requires follow-up monitoring to ensure that new safety information is obtained in a timely manner. Medical professionals should report any suspected adverse reactions. See section 4.8 for reporting information.

1. Name of the drug

MVC COVID-19 Vaccine

2. Ingredients, composition, and content

The packaging is a suspension in a pre-filled syringe.

Each dose is 0.5 ml (see section 6.5).

Each dose (0.5 ml) contains: 15μg of SARS-CoV 2 recombinant spike protein.

For a complete list of excipients, see section 6.1.

3. Pharmaceutical form

Pre-filled syringe (for intramuscular injection).

This product is a clear, colorless liquid, which becomes a turbid white suspension after inverting to mix well.

4. Clinical particulars

4.1 Indications

The MVC COVID-19 vaccine is indicated for active immunization to prevent novel coronavirus disease (COVID-19, also known as severe pneumonia with novel pathogens) in individuals 20 years of age and older.

This vaccine should be administered in accordance with the COVID-19 vaccination plan of the Central Epidemic Command Center.

Explanation:

The indications are based on the neutralizing antibody titer being comparable in amount, after two doses of the vaccine, to import products that have received special approval for use.

4.2 Posology and method of administration

Posology

Inject 0.5 ml of the MVC COVID-19 vaccine into the arm by intramuscular injection. Two doses in total are required. The second dose should be administered 28 days after the first dose.

There is no data available on the interchangeability of the MVC COVID-19 vaccine with other COVID-19 vaccines to complete the vaccination course. Those who have received the first dose of the MVC COVID-19 vaccine should be given a second dose of the MVC COVID-19 vaccine to complete the entire vaccination course.

Administration in children

The safety, antibody titer, and protective efficacy of the MVC COVID-19 vaccine for children and adolescents (<20 years old) have not yet been established. No data are available.

Administration in the elderly population

No dose adjustment is required when the MVC COVID-19 vaccine is administered in the elderly population. See sections 4.4 and 5.1.

Method of administration

Please invert the MVC COVID-19 vaccine to mix it evenly before use. It can only be administered by intramuscular injection, ideally the deltoid muscle in the upper arm.

Do not inject the vaccine intravascularly, subcutaneously, or intracutaneously.

For precautions before administering the vaccine, see section 4.4.

For disposal instructions, see section 6.6.

4.3 Contraindications

Individuals with severe allergic reactions to the active ingredient or any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

The name and batch number of the administered product should be clearly recorded in order to enhance the traceability of biological medicinal products.

Allergies and acute allergies

As with all injectable vaccines, appropriate medical treatment and supervision should be immediately available to deal with acute hypersensitivity reactions (anaphylaxis) that may occur after vaccination. After vaccination, it is recommended for vaccinees to be closely observed for at least 30 minutes. Individuals who have an acute hypersensitivity reaction after the first dose of the MVC COVID-19 vaccine should avoid receiving any more doses of the MVC COVID-19 vaccine.

Anxiety-related reactions

Anxiety-related reactions include syncope, hyperventilation caused by a vasovagal response, and other reactions caused by anxiety related to vaccine administration. Precautions should be taken. People should sit while receiving the vaccine to prevent injury from fainting.

Concurrent illness

As with other vaccines, those who are febrile or having an acute, moderate to severe illness should postpone their vaccination until their condition becomes stable. However, for minor infections and/or diseases that do not require special medical treatment, there is no need to postpone the vaccination.

Thrombocytopenia and coagulation disorder

As with other intramuscular vaccine injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or patients with thrombocytopenia or any other coagulation abnormalities (such as hemophilia), because these patients may have bleeding or bruising after receiving intramuscular injections.

Immunocompromised individuals

There is limited information on the efficacy, safety, and immunogenicity of the use of the MVC COVID-19 vaccine in immunocompromised persons (including those receiving immunosuppressant therapy). It was observed that in a small number of human immunodeficiency virus (HIV)-infected subjects, who had been taking their medication regularly and who had well-controlled viral loads in their bodies, the neutralizing antibody titers after two doses of the MVC COVID-19 vaccine were lower

than those of HIV-negative subjects. The clinical relevance of this difference in antibody titers is still unclear.

Duration of protection

As with all other COVID-19 vaccines that have received emergency authorization or approval, the MVC COVID-19 vaccine has an unknown duration of protection. It shall be determined from ongoing clinical trials.

Limitations of vaccine effectiveness

The neutralizing antibody against the SARS-CoV-2 virus raises about 2 weeks after the second dose of the MVC COVID-19 vaccine. As with all vaccines, the MVC COVID-19 may not be protective for all vaccinees.
(See section 5.1).

4.5 Interactions with other medicinal products, and other forms of interaction

No interaction-related studies have been conducted.

No studies have been conducted on concomitant administration of the MVC COVID-19 vaccine with other vaccines (e.g. flu vaccine).

4.6 Fertility, pregnancy, and lactation

Pregnancy

Currently, there is limited clinical experience on administering the MVC COVID-19 vaccine on pregnant women.

In reproduction and developmental toxicity tests in rats, a 0.5 ml vaccine dose containing 5 or 25 μg SARS-CoV 2 recombinant spike protein supplemented with 750 μg CpG 1080 and 375 μg aluminum hydroxide adjuvant was given to the female rats. The time points of vaccine administration were: one dose administered each at 3 weeks before mating, 1 week before mating, 6th day of pregnancy, 18th day of pregnancy, and 7th day of breastfeeding. The results showed that the fertility, embryonic development, and offspring development of the female rats were not affected in each dose group.

Administration of the MVC COVID-19 vaccine during pregnancy should only be considered if the potential benefits of the vaccine to the mother and fetus are higher than any potential risks.

Women who may become pregnant or are planning to become pregnant should assess the benefits and risks of vaccination.

Breastfeeding

It is not clear whether the antibodies induced by the MVC COVID-19 vaccine will be secreted in human milk.

According to the serological data from the reproduction and developmental toxicity tests, the IgG antibody against the SARS-CoV-2 recombinant spike protein may be transferred to the offspring through the milk.

There is currently no research on the impact of the MVC COVID-19 vaccine on breastfeeding infants, but in theory the vaccine will not infect mothers or infants because it is biologically inactive, so breastfeeding mothers may assess the benefits and risks of vaccination before receiving the MVC COVID-19 vaccine.

Fertility

There is currently no data related to human fertility.

According to the results of reproduction and developmental toxicity tests in rats, no damage to female fertility was observed.

4.7 Effects on ability to drive and use machines

The MVC COVID-19 vaccine has no or negligible influence on the ability to drive and use machines. However, some of the adverse reactions mentioned in section 4.8 may temporarily affect the ability to drive and use machines.

4.8 Undesirable effects

Summary of safety profile

The following safety information is based on an interim analysis of a clinical trial that is currently ongoing in Taiwan. At the time of the interim analysis, a total of 3,295 subjects over the age of 20 received at least one dose of the MVC COVID-19 vaccine, and 549 subjects received a placebo (saline solution). The median follow-up time was 63 days after the second dose of vaccine was administered. The median age of subjects vaccinated with MVC COVID-19 vaccine was 42.0 years old (range 20-89 years), of which 2,575 (78.1%) subjects were between 20 and 64 years old, and 720 (21.9%) subjects were 65 years old or older. Among the subjects given the MVC COVID-19 vaccine, males accounted for 56.3% and females accounted for 43.7%; 10.9% of subjects had a BMI≥30 kg/m^2; 6.0% were positive for hepatitis B surface antigen; 1.3% were positive for hepatitis C antibodies; 1.8% were positive for HIV antibodies; 16.7% had comorbidities. (Comorbidities are defined as cardiovascular disease, cerebrovascular disease, chronic obstructive pulmonary disease, liver cirrhosis, and higher than normal values for glycated hemoglobin A1c (HbA1c)).

The most commonly reported adverse reactions were pain/tenderness at the injection site (71.2%), fatigue/malaise (36%), myalgia (27.6%), headache (22.2%), diarrhea (15.1%), swelling/induration at the injection site (10.5%), nausea/vomiting (7.7%), erythema/redness at the injection site (4.9%), and fever (0.7%). The majority of adverse reactions were mild to moderate in intensity, and most of them become resolved or recovered within 7 days after vaccination.
According to current data, the frequency of adverse reactions observed in older subjects (≥65 years of age) was lower than that of young adults, and the incidence of serious adverse reactions was also lower than that of young adults.

Tabulated list of adverse reactions

The following safety information is based on data from placebo-controlled clinical trials conducted on 3,295 subjects aged 20 or older.

The reported adverse reactions are listed according to the following frequency convention and the Medical Dictionary for Regulatory Activities (MedDRA) system organ classes (SOC):
Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Currently unknown (Cannot be estimated based on existing data)

MedDRA SOC	Frequency	Adverse reaction
Nervous system disorders	Very common	Headache
	Common	Dizziness
		Somnolence
	Rare	Facial paralysis*
		Hypertension oculi
Cardiac disorders	Uncommon	Palpitations
Gastrointestinal disorders	Very common	Diarrhea
	Common	Nausea/Vomiting
Musculoskeletal and connective tissue disorders	Common	Myalgia
Infections and infestations	Uncommon	Nasopharyngitis
Respiratory, thoracic and mediastinal disorders	Uncommon	Oropharyngeal pain
General disorders and administration site conditions	Very common	Injection site pain
		Malaise/Fatigue
		Injection site induration
	Common	Injection site erythema
	Uncommon	Pyrexia
		Injection site pruritus
		Chills
		Rash

*During the follow-up period, there was one report of facial paralysis in the MVC COVID-19 vaccine group, which occurred 13 days after the second dose.

Reporting suspected adverse reactions

After the vaccine is authorized, its benefit/risk balance must be continuously monitored, so reporting suspected adverse reactions is very important. Healthcare professionals should report any suspected adverse reactions in accordance with the regulations of the Central Epidemic Command Center. Please also provide the batch/batch number if available.

4.9 Overdose

There are currently no cases of overdose. There are no specific treatments for an overdose with the MVC COVID-19 vaccine. In the event of an overdose, the individual's vital functions should be monitored and symptomatic treatment should be given as appropriate.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vaccine, other viral vaccine, ATC code: J07BX03

Mechanism of action

The MVC COVID-19 vaccine's antigen is a SARS-CoV-2 recombinant spike protein, and it uses CpG1018 and aluminum hydroxide as adjuvants, which can induce antibody immune responses and may contribute to protection to COVID-19.

Pharmacodynamic effect

The following immunogenicity information comes from an interim analysis of clinical trials that are currently ongoing in Taiwan.

Participants in this clinical trial include healthy subjects aged 20 or older, or subjects with stable underlying diseases. The main immunogenicity analysis group included 903 subjects who received the MVC COVID-19 vaccine and 150 subjects who received a placebo. Among the subjects administered the MVC COVID-19 vaccine, 682 (75.5%) were between 20 and 64 years old, and 221 (24.5%) were 65 years old or older. Males accounted for 57.7%, while females accounted for 42.3%; 11.6% of subjects had a BMI≥30 kg/m^2; 5.6% were positive for hepatitis B surface antigen; 1.0% were positive for hepatitis C antibodies; 1.2% were HIV positive; the rate of comorbidities was 19.3%. (Comorbidities are defined as cardiovascular disease, cerebrovascular disease, chronic obstructive pulmonary disease, liver cirrhosis, and higher than normal values for glycated hemoglobin A1c (HbA1c)).

An analysis based on an external database was performed by using a COVID-19 vaccine product that have already been approved for emergency use authorization by the Ministry of Health and Welfare in Taiwan. Among the aforementioned main immunogenicity analysis groups receiving the MVC COVID-19 vaccine, 879 subjects met the pre-defined blood sampling interval and were included in this analysis. The primary comparison subset was the subjects aged under 65 years old; the secondary comparison subset were all of the subjects.

Among the 879 subjects who received the MVC COVID-19 vaccine for analysis, the median age of the subjects was 43.0 years (range 20-87 years), 57.6% were male, and 55.2% had comorbidities (comorbidities are defined as cardiovascular disease, cerebrovascular disease, chronic obstructive pulmonary disease, liver cirrhosis, higher than normal values for glycated hemoglobin A1c (HbA1c), HIV positive, overweight and obesity, and chronic kidney disease). The proportion of males and comorbidities in the MVC COVID-19 vaccine group was higher than that in the external control group, and the differences were statistically significant. The gender and comorbidity ratio distribution of the primary comparison group is consistent with the trends of the 879 subjects, but the median age is lower (37.0 years old, range 20-64 years old).

1. Primary immunogenicity analysis compared with placebo group

The following table shows the live virus neutralizing antibody response against the prototype strain of SARS-CoV-2* in the serum of subjects compared with the placebo group 28 days after receiving the second dose of the vaccine:

Immune response indicator	MVC COVID-19 vaccine (N=903)	Placebo (N=150)
Geometric mean titer of neutralizing antibody (95% confidence interval)	662.31 (628.66, 697.75)	4.00 (4.00, 4.00)
Seroconversion rate[1] (95% confidence interval)	99.8% (99.20, 99.97)	0 (0.00, 2.43)
Geometric mean titer fold increase[2] (95% confidence interval)	163.22 (155.01, 171.87)	0.99 (0.98, 1.01)

* Prototype virus is to be distinguished from variants of concerns. The virus strain used in the test to detect the live virus neutralizing antibody titer is hCoV-19/Taiwan/4/2020.

[1] The seroconversion is defined as the proportion of the subjects in

this group with a four-fold increase in serum neutralizing antibodies 28 days after receiving the second dose of the vaccine, compared with the baseline value.
[2] The fold increase in the geometric mean titer is the multiple of the geometric mean titer of the neutralizing antibody 28 days after receiving the second dose of the vaccine, compared with the baseline value.

Administration in the elderly

The immunogenicity sub-group analysis included 221 subjects aged 65 or older who received the MVC COVID-19 vaccine and 37 subjects who received a placebo.

The following table shows the live virus neutralizing antibody response against the prototype strain of SARS-CoV-2* in the serum of subjects aged 65 or older who received the MVC COVID-19 vaccine compared with the placebo group 28 days after receiving the second dose of the vaccine:

Immune response indicator	MVC COVID-19 vaccine (N=221)	Placebo (N=37)
Geometric mean titer of neutralizing antibody (95% confidence interval)	484.54 (433.16, 542.01)	4.00 (4.00, 4.00)
Seroconversion rate[1] (95% confidence interval)	99.5 (97.50, 99.99)	0 (0.00, 9.49)
Geometric mean titer fold increase [2] (95% confidence interval)	119.75 (107.16, 133.82)	1.00 (1.00, 1.00)

* Prototype viruses are different from variants of concerns. The virus strain used in the test to detect the live virus neutralizing antibody titer is hCoV-19/Taiwan/4/2020.
[1] The seroconversion rate is defined as the proportion of the subjects in this group with a four-fold increase in serum neutralizing antibodies 28 days after receiving the second dose of the vaccine, compared with the baseline value.
[2] The fold increase in the geometric mean titer is the multiple of the geometric mean titer of the neutralizing antibody 28 days after receiving the second dose of the vaccine, compared with the baseline value.

For subjects who previously had one or more comorbidities, the average serum neutralizing antibody titer at 28 days after receiving the second dose of vaccine (N=174) was 562.92 (95% CI: 502.14; 631.05); while for the placebo group (N=31) it was 4.00 (95% CI NA).

For subjects with BMI ≥ 30 kg/m^2, the average serum neutralizing antibody titer 28 days after receiving the second dose of vaccine (N=105) was 775.34 (95% CI: 664.02; 905.33); while for the placebo group (N=15) it was 4.00 (95% CI NA).

For subjects who were HIV positive, the average serum neutralizing antibody titer at 28 days after receiving the second dose of vaccine (N=11) was 275.53 (95% CI: 170.70; 444.73); while for the placebo group (N=1) it was 4.00 (95% CI NA).

Generally speaking, for people aged 65 or older, people with comorbidities, and HIV positive subjects, although the neutralizing antibody titer was lower, the immune response trends were similar to the immune responses observed in the overall group.

2. Immunogenicity analysis in comparison with a COVID-19 vaccine product that has already been approved for emergency use authorization (EUA) by the Ministry of Health and Welfare in Taiwan as the external control

The co-primary endpoints for the predefined analysis are (1) The lower limit of the 95% confidence interval of the geometric mean titer ratio (GMTR) of the prototype strain live virus neutralizing antibodies for the MVC COVID-19 vaccine group to the external control group must be greater than 0.67, as shown in a blood test 28 days after the second dose; (2) The sero-response level was defined as the neutralizing antibody titers against the prototype strain live virus at 28 days after receiving the second dose of the vaccine, at the referred point of 60% reverse accumulative distribution curve for external control group. The lower limit of the 95% confidence interval for the sero-response rate (the proportion of subjects whose neutralizing antibody titers against the prototype strain live virus, at 28 days after receiving the second dose of the MVC-COVID-19 vaccine, are above the sero-response level) must be greater than 50%.

The analysis results showed that the lower limit of the 95% confidence interval for the GMTR of the prototype strain live virus neutralizing antibodies between the MVC COVID-19 vaccine group and the external control vaccine group was 3.4 times, which was greater than the requirement of 0.67 times. The lower limit of the 95% confidence interval for the sero-response rate of the MVC COVID-19 vaccine group was 95.5%, which was greater than the requirement of 50%.

The results of the overall group and sensitivity analysis including the elderly are consistent with the above.

Emergency Use Authorization

This product was approved to be manufactured under an emergency use authorization by the Ministry of Health and Welfare in Taiwan. This indicates that the product still needs more evidentiary support.

Any new information about this product will be reviewed by the Ministry of Health and Welfare in Taiwan, and the package insert will be updated as needed.

5.2 Pharmacokinetic properties

Not applicable

5.3 Preclinical safety data

According to preclinical data obtained from repeated dose toxicity studies in rats and reproductive and developmental toxicity studies in rats, the MVC COVID-19 vaccine causes no special hazard for humans.

Genotoxicity/carcinogenicity

Genotoxicity and carcinogenicity studies were not performed.

Reproductive toxicity

According to the results of reproduction and developmental toxicity studies in rats, no vaccine-related effects have been found on fertility in female rats, embryonic development, and the survival and development of pups.

6. Pharmaceutical particulars

6.1 List of excipients

CpG 1018
Aluminum hydroxide
Phosphate buffer solution

6.2 Incompatibilities

Do not use this drug in combination with other drugs.

6.3 Shelf life

Store in a refrigerator (2°C to 8°C). The expiration date is printed on the outer box.

6.4 Special precautions for storage

Store in a refrigerator (2°C to 8°C). Keep in the outer box to protect from light.
Do not freeze.

6.5 Nature and contents of the container

The MVC COVID-19 vaccine is a pre-filled syringe, each dose contains 0.5 ml.

6.6 Special precautions for disposal and other handling

This vaccine must be prescribed by a physician.

Do not use vaccines after the expiration date. The expiration date is printed on the outer box.

Unused pre-filled syringes should be stored in a refrigerator (2°C to 8°C). Do not freeze.

Stability data for the MVC COVID-19 vaccine shows that the pre-filled syringe may be kept and used for 3 days at a temperature of 8°C to 25°C.

Please store the pre-filled syringe in the outer box and protect from light.

Before administering the vaccine, be sure to confirm there are no particles or discoloration in the liquid and the container. The appearance of the MVC COVID-19 vaccine is a clear, colorless liquid, which becomes a turbid white suspension after inverting to mix well. Discard the pre-filled syringe if the suspension is discolored or has particles.

Version date: 2021/8/11

Manufacturer: Medigen Vaccine Biologics Corp.
Address: No. 68, Shengyi 3rd Road, Zhubei City, Hsinchu County 302

Drug producer: Medigen Vaccine Biologics Corp.
Address: No. 68, Shengyi 3rd Road, Zhubei City, Hsinchu County 302
Telephone: (03)668-4866