FACT SHEET FOR HEALTHCARE PROVIDERS ADMINISTERING CORONAVAC VACCINE TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19) (VACCINATION PROVIDERS)

BACKGROUND

The Drug Control Authority of Malaysia has allowed for the conditional registration of pharmaceutical products including vaccines with a validity period of one (1) year to provide expedited access to products for treatment or prevention of diseases during disasters without compromising aspects of quality, safety and efficacy using a risk-based approach.

Vaccines which are conditionally registered under this procedure will be subjected to the Lot Release requirements before the vaccines can be distributed in Malaysia. This is to ensure each of the batches was consistently produced according to the required quality, safety and efficacy standards as set during the approval process.

DESCRIPTION OF COVID-19 INFECTION

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, SARS-CoV-2 that was first detected in Wuhan, China in late 2019. It is predominantly a respiratory illness that can affect other organs.

The severity of COVID-19 symptoms can range from very mild to severe. Some people may have only a few symptoms, and some people may have no symptoms at all. Some people may experience worsened symptoms, such as worsened shortness of breath and pneumonia, about a week after symptoms start. Symptoms which have been commonly reported include: fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhoea.

People who are older have a higher risk of serious illness from COVID-19, and the risk increases with age. People who have existing chronic medical conditions also may have a higher risk of serious illness.

PRODUCT INFORMATION

Brand Name	:	CoronaVac
Product Name	:	CoronaVac Suspension for Injection COVID-19 Vaccine (Vero Cell), Inactivated
Manufacturer	:	Sinovac Life Sciences Co. Ltd., P.R China
Product Registration Holder	:	Pharmaniaga LifeScience Sdn Bhd

CoronaVac is a COVID-19 vaccine developed by the biopharmaceutical company Sinovac Life Sciences Co. Ltd., P.R China. It is an inactivated vaccine produced through a process where the novel coronavirus (CZ02 strain) is inoculated with the African green monkey kidney cells, and made through culture and virus solution harvest, virus inactivation, concentration, purification and aluminium hydroxide adsorption. The novel coronavirus (SARS-CoV-2) is the main component, and its auxiliary materials are aluminium hydroxide, disodium hydrogen phosphate, monosodium dihydrogen phosphate, sodium chloride and water for injection. CoronaVac does not contain alcohol or any preservative.

CoronaVac clinical trials have been conducted in China and other countries including Brazil, Chile, Indonesia and Turkey. Several findings from these studies have been published in the public domain.

CoronaVac is indicated for active immunization to prevent COVID-19 caused by SARS CoV-2 in individuals 12 years of age and older. It is intended to be used to combat the COVID-19 pandemic which has affected Malaysia since early 2020. Based on Phase I/II study and phase II(b) study conducted in China, phase III study conducted in Brazil, Indonesia and Turkey as well as phase III(b) bridging trial in different production scales and different populations suggests that CoronaVac is well tolerated and safe to be administered to paediatrics (aged 12-17 years), adults (aged 18-59 years), and elderly (aged 60 years and above) populations.

Immune-bridging on neutralizing antibody comparison was conducted to compare the seropositive rate and Geometric Mean Titres (GMT) response of vaccinated subjects in the paediatric, adult and elderly populations using minimum cut-off non-inferior margin of (-)10% for seropositive rate and a GMT ratio (GMR) margin of 0.67.

Neutralizing antibodies level, after completion of 2-dose vaccination is identified as suitable biomarkers to infer Covid-19 vaccine effectiveness from adults to paediatric populations via immunobridging. Serum samples were obtained from Phase I/II clinical trials in the elderly, Phase I/II clinical trials in children and adolescents aged 3-17 years old and Phase IIIb clinical trials in adults.

The results of the study shows that the immunogenicity response of adolescents and children vaccinated according to the 0,28-day schedule is superior to immunogenicity response in adults who were vaccinated with 0,14-day schedule. The immunogenicity response in elderly vaccinated according to the 0,28-day schedule is non-inferior to that of adults vaccinated according to the 0,14-day schedule. The study successfully demonstrated that CoronaVac produces comparable immune response in children, adolescents and elderly according to 0,28-day schedule to that of adults.

There is limited data on the use of CoronaVac in individuals ≥ 60 years of age. CoronaVac, when administered to individuals ≥ 60 years of age, has shown adequate and similar neutralizing antibodies titres as in adults. At present, it is recommended that vaccination for people aged 60 and above should be considered cautiously and its necessity should be evaluated based on their health condition and exposure risk.

Based on safety and immunogenicity data of phase I/II clinical trial in individuals 18 years of age and older, the booster dose immunization was performed 6 months after the 2-doses primary immunization. The immunogenicity response in adults and elderly vaccinated with booster dose according to the 0,28-day schedule are non-inferior with primary immunization. The level of neutralizing antibody was significantly increased suggesting a better immune memory response.

Following to Phase III clinical trial conducted in Brazil, Turkey and Indonesia of CoronaVac with 0,14-day schedule, the result of efficacy analysis of the vaccine was 50.65%, 91.90% and 51.98% according to the case definition recommended by National Medical Products Administration (NMPA) respectively.

To date, CoronaVac has been approved for emergency use in at least 49 countries such as China, Hong Kong, Turkey, Indonesia, Cambodia, Brazil, Mexico, Paraguay, Chile, Commonwealth of Dominica, Zimbabwe, Ecuador, Tunisia, Pakistan, Ukraine, Morocco, Egypt, UAE, Oman, South Africa, Philippine, Thailand, Myanmar, Columbia, Algeria and Djibouti for the immunization of the general public against COVID-19 infections. The product has received conditional approval in China as of 5th Feb 2021.

The information stated on inner and outer carton labels of CoronaVac is based on the global label. For Malaysian-specific information, please refer the NPRA-approved package insert

SUMMARY OF INSTRUCTIONS FOR CORONAVAC VACCINATION PROVIDERS

Healthcare workers involved in the nationwide immunization program to counter COVID-19 in Malaysia must report all adverse events following immunization (AEFI) including any Vaccine-Associated Enhanced Disease (VAED) following administration of CoronaVac. The vaccination provider is responsible for mandatory reporting of the following to the National Pharmaceutical Regulatory Agency (NPRA):

- serious*** AEFI (irrespective of attribution to vaccination)
- vaccine administration errors whether or not associated with an adverse event
- non-serious AEFI

*** *Serious adverse events / AEFI are defined as those that cause:*

- *death*
- *life-threatening*
- *inpatient hospitalization or prolongation of existing hospitalization*
- *persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions*
- *congenital anomaly/birth defect*
- *an important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent one of the outcomes listed above.*

Complete reports with information on the vaccine recipient (without divulging confidential information), detailed description of the adverse event, batch number of the vaccine and other information as required on the AEFI reporting forms. The following forms can be used to report AEFI:

- *Report on Suspected Adverse Drug Reaction* form (also commonly known as the '*blue form*') or
- *Borang Pemantauan Kesan Advers Ringan Susulan Imunisasi*

Either form should be submitted either online or manually in a timely manner to the National Centre for Adverse Drug Reaction Monitoring. You may access these forms and an ADR reporter guide via npra.gov.my [Health professionals → Reporting ADR] or scan the QR code below:

Information on AEFIs should also be provided to the marketing authorisation holder when requested to enable them to compile and further analyse safety data pertaining to CoronaVac as this is a condition imposed upon them by the regulatory authority.

STORAGE AND HANDLING

CoronaVac is supplied in box of 40 vials.

Unopened vial (single dose and multi-dose)

CoronaVac must be stored at a temperature between 2°C to 8°C, protect from light. Do not freeze.

Multi-dose vial

After first puncture, the vaccine (vial) can be stored at 2°C to 8°C for up to 6 hours or at room temperature (maximum 37°C) for a single period of up to 1 hour. Discard any unused vaccine if it is not kept within the recommended conditions.

All cartons will be supplied with a Cold Chain Monitor (CCM) device for temperature monitoring to ensure that there is no break in the cold chain throughout the supply chain. The CCM is a device that will detect any temperature excursions beyond 2°C to 8ºC. It will be used throughout the cold chain supply of the CoronaVac vaccine.

SHELF LIFE

Unopened vial (single dose and multi-dose)

18 months.

Multi-dose vial

For shelf-life after first puncture, refer section **Storage and Handling**.

DOSAGE AND ADMINISTRATION

CoronaVac is available as a single dose and multi dose in the following presentations:

- Single-dose (1 dose) vial of 0.5 mL
- Multi-dose (2 doses) vial of 1.0 mL

Each dose (0.5 mL) contains 600SU (equivalent to 3µg) of inactivated SARS-CoV-2 antigen.

No dosage adjustment is required when administered to individuals age 12 years and above.

To achieve optimal immunization, two doses need to be administered intramuscularly with the second dose of the same vaccine. A booster dose (0.5 mL) is recommended to be administered at least 3-6 months after the second dose in individuals 18 years of age and older.

Recommended dosing interval (primary immunization)	
Adolescents (12-17 years old)	**Adults (≥ 18 years old)**
28 days after first dose	14 - 28 days after the first dose

Shake the vial and visually inspect prior to administration. The vaccine will be an opalescent aqueous solution. Do not administer if vaccine is discoloured or contains any particulate matter.
The injection should be administered intramuscularly into the deltoid muscle. It should not be administered intravenously. There is no safety or efficacy data on subcutaneous or intradermal injection.

CONTRAINDICATIONS

- Individuals who are hypersensitive or known to be allergic to any of the components of CoronaVac vaccine or similar vaccines
- Previous severe allergic reactions to the vaccine (e.g. acute anaphylaxis, angioedema, dyspnoea)
- Individuals with severe neurological conditions (e.g. transverse myelitis, Guillain-Barré syndrome, demyelinating diseases)
- Individuals with uncontrolled severe chronic disease

WARNINGS

As with all other vaccines, there is a possibility of anaphylactic reaction occurring in the vaccine recipient. Appropriate medical treatment including adrenaline injection and emergency treatment used to manage allergic reactions and anaphylaxis must be immediately available at the place of administration.

Vaccine recipients should be asked to wait at the site for 30 minutes post administration to enable close monitoring for any untoward immediate adverse reactions.

CoronaVac vaccine may not offer protection against contracting the COVID-19 infection in all vaccine recipients. Some individuals may have a diminished immune response for a variety of reasons such as immunocompromised persons. Good hygiene, wearing of face masks especially amongst high-risk individuals and physical distancing may still need to be adhered to until the infection rate is well controlled.

SPECIAL POPULATION MEDICATION

Pregnancy

Limited experience exists with use of CoronaVac in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development. Administration of CoronaVac in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus.

Breastfeeding

It is unknown whether CoronaVac is excreted in human milk.

Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

ADVERSE REACTIONS

Adverse event frequencies are based on the grading standard of adverse reaction incidence from Council for International Organizations of Medical Sciences (CIOMS): 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), not known (cannot be estimated from the available data).

Adverse reactions for both primary vaccination schedule and booster dose which have been reported with CoronaVac from clinical trials are as follows:

Very common	Common	Uncommon	Rare
Localized (Injection Site) Reactions			
• pain	• swelling	• burning sensation • vaccination site discolouration • pruritus • erythema • induration • injection site hypoaesthesia	-
Systemic Reactions			
-	• fatigue • myalgia • nausea • diarrhoea • arthralgia • cough • chills • rhinorrhoea • sore throat • nasal congestion • fever • headache	• vomiting • hypersensitivity • abnormal skin and mucosa • tremors • flushing • oedema • dizziness • drowsiness • abdominal pain • abdominal distension • decrease of appetite • erythema • pruritus • papule	• muscle spasms • periorbital oedema • nose bleed/ epistaxis • constipation • hyposmia • ocular congestion • hot flushes • hiccups • conjunctival congestion

Additional information with regard to breakthrough infections, rare and delayed adverse reactions may become apparent with more widespread use of CoronaVac. Vaccine recipients should be advised to report any adverse events which may be experienced directly to the healthcare professionals at the healthcare facility where the vaccine was administered or to the National Centre for Adverse Drug Reaction Monitoring by visiting the website www.npra.gov.my [Consumers → Reporting Side Effects to Medicines (ConSERF) or Vaccines (AEFI)].

USE WITH OTHER VACCINES

Currently, there is no information on the co-administration of CoronaVac with other vaccines. Data will be compiled with more widespread use of CoronaVac and subsequent studies involving this vaccine.

INFORMATION TO PROVIDE TO VACCINE RECIPIENTS/CAREGIVERS

As the vaccination provider, you are advised to communicate to the vaccine recipient or their caregiver, information consistent with the Product Information, Patient Information Leaflet and Fact Sheet for Recipients and Caregivers prior to the individual receiving each dose of CoronaVac vaccine, including:

- The Drug Control Authority has authorized the conditional use of CoronaVac to combat the current pandemic based on current available scientific without compromising on the safety, quality and efficacy of the products
- Vaccination is not compulsory and the vaccine recipient or their caregiver has the option to accept or refuse CoronaVac
- Based on current scientific data, the benefits of vaccination outweigh its risks. However, long term safety data for CoronaVac is not yet available
- Currently, there is no approved alternative treatment to prevent COVID-19
- To obtain optimal efficacy, the vaccine has to be administered twice. The recommended interval after the first dose for adolescents is 28 days and for adults is 14-28 days.
- It is recommended to conduct booster immunization at an interval of at least 3-6 months.
- It is not advisable to use different brands of the vaccine for the first and second dose as there is are significant differences between the currently available COVID-19 vaccines

Vaccine recipients/caregivers will be provided with a Vaccination Reminder Card with the date when the recipient needs to obtain the second dose of CoronaVac vaccine. Advice should be provided on action to be taken should they not be able to come on the appointed date.

ADDITIONAL INFORMATION

For general questions and additional information pertaining to CoronaVac vaccine, please visit The Special Committee for Ensuring Access to COVID-19 Vaccine Supply (JKJAV) website at www.vaksincovid.gov.my

INSTRUCTION FOR USE

Shake before use.

Inspect visually prior to administration.

The vaccine should not be used if foreign particles are present in the suspension.

Upright position tilted at 45° is recommended to withdraw 0.5 mL of each vaccine dose into a 1mL Low-Dead-Volume (LDV) syringe. The LDV syringe and needle combination should have a dead volume of no more than 0.05mL.

Use a separate sterile needle and syringe for each individual dose. Aseptic techniques should be used when withdrawing each dose of the vaccine.

Recommended needle sizes for vaccine withdrawal: 21G with the length size at least 38mm ($1\frac{1}{2}$").

Recommended needle size for vaccination: 25G / 25mm.

Vaccine should be administered immediately after withdrawal from the vial.

For multi-dose vials, precautions must be taken to avoid contamination of the vial content.

Any excess volume inside the vial after the first withdrawal to be extracted completely to ensure the amount of vaccine meet the 0.5 mL dose for the second injection.

If there is insufficient volume withdrawn, check if there is any more vaccine residual leftover in the vial at upright position for at least 30 seconds.