DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION (DHPC)

PRODUCT NAME: CORONAVAC SUSPENSION FOR INJECTION SARS-CoV-2 VACCINE (VERO CELL), INACTIVATED

REGISTRATION NO: MAL21036010ARZ

Dear Healthcare Professional,

Please be informed that details in the vial label (immediate label) and outer carton label for CoronaVac are based on the global product information issued by the manufacturer, Sinovac Life Sciences Co., Ltd., P.R. China.

However, product details specified in the Package Insert (PI) and Patient Information Leaflet (PIL) are based on information approved by Drug Control Authority (DCA), Malaysia. As such, there are differences of information in the product vial label, outer carton label, package insert and PIL as follows:

<table>
<thead>
<tr>
<th>Details</th>
<th>Global Label (vial and outer carton)</th>
<th>Label Approved by DCA, Malaysia (PI and PIL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product Name</td>
<td>CoronaVac COVID-19 Vaccine (Vero Cell), Inactivated</td>
<td>CoronaVac Suspension for Injection, SARS-CoV-2 Vaccine (Vero Cell), Inactivated</td>
</tr>
<tr>
<td>Indication</td>
<td>This vaccine is indicated in population aged 18 years and over. COVID-19 Vaccine (Vero Cell), Inactivated can stimulate body to induce immunity against the disease caused by SARS-CoV-2 virus.</td>
<td>CoronaVac is indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2, in individuals 18 years of age and older. The use of this vaccine should be in accordance with official recommendations.</td>
</tr>
<tr>
<td>Dose</td>
<td>The immunization schedule is 2 doses at 2-week interval.</td>
<td>Two doses should be administered for primary immunization. The second dose is preferably given 14 – 28 days after the first dose. 0.5 mL per dose. It has not been determined whether this product requires booster immunization.</td>
</tr>
<tr>
<td>Shelf life (from date of manufacture)</td>
<td>36 months (by way of expiry date)</td>
<td>9 months</td>
</tr>
</tbody>
</table>

For the avoidance of doubt, all government facilities are advised to refer ONLY to the information in the product PI and PIL, which is specific for use of CoronaVac in the Malaysian population.

Please take note that the shelf life approved by DCA, Malaysia for CoronaVac is 9 MONTHS. Therefore, upon receipt of CoronaVac supply, government facilities are advised to transcribe the actual expiry date onto the vial label. The actual expiry date is calculated as a period of 9 MONTHS (approved shelf life) from the product manufacturing date. The product manufacturing date can be found on the outer carton label.

The communication of this information has been agreed with National Pharmaceutical Regulatory Agency (NPRA), Ministry of Health Malaysia.

Thank you.

Yours sincerely,

Vanessa Daniel

Responsible Person for Pharmacovigilance (RPPV)
Pharmaniaga LifeScience Sdn Bhd
CoronaVac Suspension for Injection SARS-CoV-2 Vaccine (Vero Cell), Inactivated

CONTROLLED MEDICINE / UBAT TERKAVAL

DISCLAIMER: THIS PRODUCT IS APPROVED UNDER MALAYSIA CONDITIONAL REGISTRATION FOR PHARMACEUTICAL PRODUCTS DURING DISASTER GUIDELINE. THE ADMINISTRATION OF THE PRODUCT IS PURELY BASED ON INDIVIDUAL’S PREFERENCE.

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected new or serious adverse reactions.

This product information will be updated on a regular basis as further data and safety reports become available.

The information stated on inner and outer carton labels is based on the global label. For Malaysia specific information, please refer to this package insert.

COMPOSITION
Each dose (0.5 mL) contains 600 SU (equivalent to 3µg) of inactivated SARS-CoV-2 antigen.
Excipient: Aluminum hydroxide, disodium hydrogen phosphate, monosodium diphosphoglycinate, sodium chloride, sodium hydroxide and water for injection.

No preservative in this product.

DESCRIPTION
CoronaVac is a milky-white (opalescent) suspension. Strawfied precipitate may form which can be dispersed by shaking.

INDICATION
CoronaVac is indicated for active immunization to prevent COVID-19 caused by SARS-CoV-2, in individuals 18 years of age and older.

The use of this vaccine should be in accordance with official recommendations.

RECOMMENDED DOSAGE
Individuals 18 years of age and older
Two doses should be administered for primary immunization. The second dose is preferably given 14 - 28 days after the first dose. 0.5 mL per dose. It has not been determined whether this product requires booster immunization.

Paediatric population
The safety and efficacy of CoronaVac in children and adolescents aged less than 18 years of age have not yet been established. No data are available.

Elderly population
No dosage adjustment is required in elderly individuals ≥ 60 years of age.

There is limited data on the use of CoronaVac in individuals ≥ 60 years of age, CoronaVac, when administered to in 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 cautiously considered, its necessity should be evaluated based on their health condition and expatriate risk.

Method of administration
CoronaVac should be administered by intramuscular injection in the deltoid region of the upper arm.

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.
The vaccine should be used immediately after opening.

ROUTE OF ADMINISTRATION
Intramuscular injection.

CONTRAINDICATIONS

1. Individuals who are hypersensitive or known to be allergic to any component (active ingredients or excipients or any material used in process) of the vaccine or similar vaccines;
2. Previous severe allergic reactions to the vaccine (e.g., acute anaphylaxis, angioedema, dyspnea);
3. Individuals with severe neurological conditions (e.g., transverse myelitis, Guillain-Barré syndrome, demyelinating diseases);
4. Individuals with uncontrolled severe chronic diseases;
5. Pregnant and lactating women

WARNINGS AND PRECAUTIONS
1. There is limited data on the duration of protection afforded by the vaccine. As such, necessary protective measures should be taken in line with the COVID-19 epidemic.
2. This vaccine should under no circumstances be administered intravascularly. There are no safety or efficacy data for administration of CoronaVac via subcutaneous or intradermal routes.
3. As with all injectable vaccines, appropriate supervision and treatment including adrenaline injection and emergency care should always be readily available in case of an anaphylactic reaction following the administration of the vaccine. Individuals should be observed for at least 30 minutes on site after vaccination.
4. Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. It is important that precautions are in place to avoid injury from fainting.
5. CoronaVac should be used with caution in individuals with acute diseases, acute exacerbation of chronic diseases, severe chronic diseases, allergies and fever. If necessary, vaccination should be delayed upon doctor’s assessment.
6. CoronaVac should be used with caution in individuals with diabetes, convulsions, epilepsy,encephalopathy and mental illness or family history of mental illness.
7. Further use of CoronaVac should be avoided in individuals who experience adverse effects related to the nervous system following administration.
8. As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) as bleeding or bruising may occur following an intramuscular administration in these individuals.
9. The safety and efficacy, of the vaccine has not been assessed in those with impaired immune function (patients with malignant tumour, nephrotic syndrome, AIDS) including those receiving immunosuppressant therapy. Use of CoronaVac in these individuals should be considered in consideration of a potentially lowered immune response.
10. Human immunoglobulin injections should be given at least one-month interval before or after the administration of the vaccine to avoid lowered immune response.
11. Do not use if there are cracks, spots, stains and scratches on the outer surface of the glass vial or if label is not clear.
12. Do not mix CoronaVac with other vaccines in the same syringe.
13. Avoid exposure of CoronaVac to disinfectants during use.
14. Do not freeze. It shall be administered immediately after opening.
15. This product should be stored out of reach of children.
16. As with any vaccine, the protective effect of CoronaVac may not reach 100% for all recipients.

INTERACTIONS WITH OTHER MEDICAMENTS
Concomitant administration of other vaccines: No interaction studies have been performed.
There are no clinical studies on the concomitant (pre, post or simultaneous) use of CoronaVac with other vaccines.

Immunosuppressive drugs: The use immunosuppressive drugs such as immuno inhibitors, chemotherapyna drugs, antimitobolites, alkylation agents, cytotoxic drugs and corticosteroids may lower the immune response of CoronaVac. The use of CoronaVac in individuals receiving immunosuppressive treatments and/ or drugs should be determined by a doctor.

Incompatibility
This vaccine shall not be mixed with the other vaccines in the same syringe.

PREGNANCY AND LACTATION
CoronaVac is contraindicated in pregnant and lactating women. There is limited information on the use of CoronaVac in pregnant and lactating women.

ADVERSE EFFECTS
The safety of CoronaVac was evaluated in 4 clinical trials conducted in China and other countries, including randomized, double-blind, placebo-controlled phase III clinical trials in people aged 18-59 years and in elderly aged 60 years and above, a phase III clinical efficacy trial in Brazilian health professionals aged 18 years and above, and a phase III bridging trial in different production scales and different populations.

Systematic safety observation was carried out within 7 days after each vaccination, and adverse events were collected by voluntary report of subjects and regular follow-up of investigators on 8-14/28 days, long-term of serious adverse events.
within 12 months after the full vaccination is still ongoing.

General description of adverse reactions in clinical trials of this product
A total of 14,572 subjects aged 18 and above were enrolled in a series of clinical trials conducted domestic and overseas, of which 7,658 subjects received at least one dose. All subjects have completed at least 28 days follow-up after full immunization, and long-term safety visits are ongoing.

Adverse event frequencies are based on the grading standard of adverse reaction incidence from Council for International Organizations of Medical Sciences (CIOMS). Very common (≥1/100); common (≥1/100 to <1/10); uncommon (≥1/10,000 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).

All adverse reactions are summarized and described as follows.

Localised (Injection Site) adverse reactions
Very common: pain
Common: swelling, pruritus, erythema, induration
Uncommon: burning sensation

Systemic adverse reactions
Very common: headache, fatigue
Common: myalgia, nausea, diaphoresis, arthralgia, cough, chills, pruritus, loss of appetite, rhinorrhea, sore throat, nasal congestion, abdominal pain
Uncommon: vomiting, hypersensitivity, abnormal skin and mucosa, fever, tremors, flushing, oedema, dizziness, drowsiness
Rare: muscle spasms, periorbital oedema, nose bleed/spistaxis, abdominal distension, constipation, hyposmia, ocular congestion, hot flushes, hiccups, conjunctival congestion

OVERDOSE AND TREATMENT
In the Phase III clinical trials, 286 adults and 245 elderly subjects were administered with high dosage of CoronaVac (1200SUI/dose/0.5mL).

There were no significant differences in the overall adverse reaction observed between adults and elderly. Most of the adverse reactions were mild and moderate, indicating that the safety of high dosage of CoronaVac is favourable.

In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINE
CoronaVac has no or negligible influence on the ability to drive and use machines. However, some of the adverse may temporarily affect the ability to drive or use machines.

PHARMACODYNAMICS
Mechanism of Action
CoronaVac has been developed by inactivating SARS-CoV-2 coronavirus, which is isolated from COVID-19 infected patient in China. The virus seed was cultured in large-scale Vero cells factories, and inactivated to make it inactive and unable to replicate in vivi, but still maintain the structural integrity of virus particles. The purified viruses were mixed with Al(OH)₃ adjuvant and served as SARS-CoV-2 vaccine. Viral structural proteins, including spike protein (S-protein) can activate the immune system and produce neutralizing antibodies which may contribute to protection against COVID-19 infection.

Immunogenicity
In Phase III study in healthy adults, safety, tolerability and immunogenicity of 3µg and 6µg dose is evaluated at different dosing schedules. Study demonstrated 92% seroconversion for neutralizing antibody titres in 2-dose vaccination schedule at 0, 14 days with 3µg / 0.5 ml, which was comparable to high dose of 6µg / 0.5 ml. In addition, study demonstrated 97% seroconversion for neutralizing antibody titre for 3µg / 0.5 ml dose administered at 0, 28-day schedule.

In another Phase III study in elderly population of age 60 years and above, safety and immunogenicity of vaccine is evaluated in 0, 28-day schedule. The seroconversion rates (±1.8) in 3µg and 6µg dose arm were 97.96% and 98.98% respectively.

Efficacy
In Phase III, multicentre, randomised clinical study in high-risk Health care population in Brazil, two-doses vaccination of CoronaVac at 0,14-day schedule. Results showed in the efficacy analysis of this clinical trial, total efficacy of the vaccine was 50.65% (95% CI: 35.66, 62.15) according to the case definition recommended by NMPA, China.

Efficacy results to the cases of different severity showed that for Grade 3 and above grades confirmed cases could achieve efficacy of up to 83.70% (95% CI: 57.99, 93.67). Effect for Grade 4 and above confirmed cases and severe patients could achieve efficacy of 100% (95% CI: 58.53, 100.00) and 100% (95% CI: 16.95, 100.00) respectively, which shows a great protective effect on moderate and severe cases. This could achieve efficacy standard for protective effect of ≥ 50% (95% confidence with interval lower limit ≥ 30%) as recommended by WHO.

In an ongoing study in Turkey in which 12,450 subjects were expected to be enrolled. As of December 23, 2020, a total of 9,190 subjects from 24 clinical trial sites screened for enrolment and 7,971 subjects (4,750 participants in Vaccine group, 64.6%; 2,621 participants in Placebo group, 35.4%) were randomized into groups, a total of 10,826 doses vaccines was administered. Official interim analysis is still pending.

In another ongoing study in Indonesia, interim efficacy evaluation of 2 doses of CoronaVac in preventing COVID-19 was conducted (study up to 6 months after the second dose of injection) based on the primary efficacy endpoint for all subjects with a data cut-off of January 9, 2021. Efficacy in preventing symptomatic confirmed cases of COVID-19 occurring at least 14 days after the second dose of vaccine was found to be 65.30% (95% CI: 16.91, 85.51).

PHARMACOKINETICS
Not applicable.

PRECLINICAL SAFETY DATA
Non-clinical data reveal no special hazard for humans based on conventional studies of single dose toxicity, repeat dose toxicity, local tolerance and systemic active anaphylaxis test.

Genotoxicity/Carcinogenicity
Neither genotoxicity nor carcinogenicity studies were performed. The components of the vaccine are not expected to have genotoxic potential.

Reproductive Toxicity
Reproductive and developmental toxicity were investigated in male and female rats in a fertility and developmental toxicity study. Both male and female rats were intramuscularly administered with CoronaVac prior to mating. No significant adverse reaction was observed on the fertility of parental female and male rats, and gestation/lactation female rats. No embryo-fetal developmental toxicity and teratogenicity or effect on the growth and development of F1 pups was observed.

STORAGE CONDITIONS
Store between +2°C to +8°C and protect from light. Do not freeze.

Keep medicine out of reach of children.

SHELF LIFE
9 months.

DOSE FORMS AND PACKAGING AVAILABLE
This product is packaged into vial, 40 vials per box.

PRODUCT REGISTRATION HOLDER
Pharnamiga LifeScience Sdn Bhd (198201009299)
Lot 7, Jalan PPU 3, Taman Perindustrian Puchong Utama, 47100 Puchong, Selangor, Malaysia

MANUFACTURER
Sinovac Life Sciences Co., Ltd.
No. 21, Tianfu Street, Daxing Biomedical Industrial Base of Zhongguancun Science Park, Daxing District, Beijing, P.R. China.

REGISTRATION NUMBER
MAL21036010ARZ

DATE OF REVISION
18th March 2021

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ARTWORK LOG
Please Chop & Sign For Approval
Revision no. Date Reason for Change
01 09.03.2021 - New artwork received, amend logo to b/w, add in 2003863
02 10.03.2021 - Move 2003863 after Date of Revision and remove red line.
03 17.03.2021 - Amend wording and registration no.
04 18.03.2021 - Amend wording and date of revision.