Central Drugs Standard Control Organization

Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India
FDA Bhavan, ITO, Kotla Road, New Delhi -110002

Annexure - III

SUMMARY OF TECHNICAL EVALUATION REPORT

(PUBLIC ASSESSMENT REPORT)

COVID-19 Vaccine, Adjuvanted 2023-2024 Formula [SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine, Omicron XBB.1.5 variant] (COVOVAX)

M /s. Serum Institute of India Pvt. Ltd. Pune

1. **Generic Name:**
   COVID-19 Vaccine, Adjuvanted 2023-2024 Formula [SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine, Omicron XBB.1.5 variant] (COVOVAX).

2. **Description & Dosage Form:**
   Dispersion for injection

3. **Presentations approved:**
   Multi-dose presentation

4. **Composition (components and its quantity per dose):**
   One dose (0.5 mL) contains
   SARS-CoV-2 (Omicron XBB.1.5) spike protein*…. 5 micrograms
   Matrix-M**: Fraction-A…..42.5 micrograms
   Matrix-M**: Fraction-C……7.5 micrograms
   *produced by recombinant DNA technology using a baculovirus expression system in an insect cell line that is derived from *Sf9* cells of the *Spodoptera frugiperda* species
   ***Quillaja saponaria* Molina extract.
   The other ingredients are Disodium hydrogen phosphate heptahydrate, Sodium dihydrogen phosphate monohydrate, Sodium chloride, Polysorbate 80 and Water for injections.

5. **Approved Indication of the vaccine:**
   For active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older.

6. **Posology of vaccine:**
   The vaccine is indicated for active immunization to prevent COVID-19 disease
   a) In individuals of ≥ 12 to < 18 years of age as primary series of two doses (0.5 mL each) 3 weeks apart
   b) As single precautionary dose in individuals of ≥ 18 years of age, who have received primary series of vaccinations.

7. Instructions for administration

Each 0.5 mL dose is withdrawn into a sterile needle and sterile syringe to be administered by intramuscular injection, preferably in the deltoid muscle of the upper arm.

Do not mix the vaccine in the same syringe with any other vaccines or medicinal products. Do not pool excess vaccine from multiple vials. Store the opened vial between 2°C to 8°C for up to 12 hours or at room temperature (maximum 25°C) for up to 6 hours after first puncture.

8. Handling of multi dose vials

Inspect the vial; gently swirl the multidose vial before and in between each dose withdrawal. Do not shake. Each multidose vial contains a colourless to slightly yellow, clear to mildly opalescent dispersion free from visible particles. Visually inspect the contents of the vial for visible particulate matter and/or discolorations prior to administration. Do not administer the vaccine if either are present.

9. Concomitant medication (If any)

Concomitant administration of COVID-19 Vaccine XBB.1.5 with other vaccines has not been studied.

10. Precautions for use

- Events of anaphylaxis have been reported with COVID-19 vaccine (Original, Wuhan strain). Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following the administration of the vaccine.
- There is an increased risk of myocarditis and pericarditis following vaccination with COVID-19 vaccine (Original, Wuhan strain). These conditions can develop within just a few days after vaccination and have primarily occurred within 14 days.
- Vaccination should be postponed in individuals suffering from an acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination.
- 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) because bleeding or bruising may occur following an intramuscular administration in these individuals.
- The efficacy, safety, and immunogenicity of the vaccine has been assessed in a limited number of immunocompromised individuals.

11. Storage conditions

Unopened vaccine should be stored at 2°C to 8°C and kept within the outer carton to protect from light.

12. Shelf life approved

12 months at 2°C to 8°C, protected from light. Unopened COVID-19 Vaccine has been shown to be stable up to 12 hours at 25°C.

13. Precautions for storage (If any)

Unopened COVID-19 Vaccine has been shown to be stable up to 12 hours at 25°C.

Punctured vial may be stored 12 hours at 2°C to 8°C or 6 hours at room temperature (maximum 25°C) from the time of first needle puncture to administration.

14. Brief description on container closure of drug product

The vaccine will be supplied as ready to use liquid in rubber-stoppered 5-dose vial presentation (2.5 mL per vial)

15. Regulatory Status in India and other Countries:

India

The parent vaccine (Wuhan Strain) is approved for restricted use in emergency situation in the country for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 7 years of age and older. Approved for administration of heterologous booster dose to individuals > 18 years of age, vaccinated with primary vaccination with COVISHIELD & COVAXIN.

The vaccine with Strain updated as Omicron XBB.1.5, is approved for restricted use in emergency situation in the country for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older.

Overseas

1. WHO Emergency Use Listing approval dated 22.11.2023 for Nuvaxovid (COVID 19 Vaccine, Recombinant, adjuvanted) with a subvariant of the SARS-CoV-2 virus (Omicron XBB.1.5),
2. EMA approval dated 31.10.2023 for use in adults and children from 12 years of age,
3. USFDA Emergency Use Authorization dated 03.10.2023 for the product NOVOVAX COVID-19 Vaccine, Adjuvanted (2023-2024 Formula) containing the recombinant spike (rS) protein from the SARS-CoV-2

Omicron variant lineage of XBB.1.5 active immunization to prevent the COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older,

4. Health Canada Notice of Compliance dated 05.12.2023 for the product Nuvaxovid XBB.1.5 (COVID-19 Vaccine (Recombinant protein, Adjuvanted) for active immunization to prevent the COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older,
5. TGA Australia dated 09.11.2023.

16. The country of origin of imported product, responsible NRA and address (not applicable for indigenous vaccine)

Not applicable as the vaccine is technology transfer from M/s Novavax, USA.

17. Brief summary and conclusion of safety & Immunogenicity/efficacy of Phase I, II and III clinical trials separately

Overseas Clinical trials:

1. The safety of COVID-19 vaccine (Original, Wuhan strain), the monovalent vaccine (Omicron BA.1) and the bivalent vaccine (Original and Omicron BA.1) administered as a booster dose to individuals 18 through 64 years of age, previously vaccinated with three doses of an authorized or approved mRNA COVID-19 vaccine was assessed in a randomized, observer blind study in Australia). The most frequent solicited adverse reactions in those receiving Monovalent Vaccine (Omicron BA.1) were injection site pain/tenderness (69.3%), fatigue/malaise (44.9%), muscle pain (25.1%), headache (37.5%), and joint pain (9.5%). A comparable safety profile was seen across all vaccine groups.

   Immunogenicity:

   Neutralizing antibody titers for the Omicron BA.1 virus, measured by a microneutralization assay [MN50], were evaluated at 14 days after vaccination. Participants included in the day 14 per protocol analysis set population (n=240) had no serologic or virologic evidence of SARS-CoV-2 infection prior to the booster dose.

   The GMTs were 318.2 (95% CI: 269.8, 375.3) in the monovalent vaccine (Omicron BA.1) group (n= 247) and 218.1 (95% CI: 186.0, 255.7) in the COVID-19 vaccine (Original, Wuhan strain) group (n= 244), resulting in an estimated GMT ratio of the monovalent vaccine (Omicron BA.1) versus the COVID-19 vaccine (Original, Wuhan strain) of 1.5 (95% CI: 1.36, 1.77). The seroresponse rates (percentage) were 54.3% in the monovalent vaccine (Omicron BA.1) group and 32.0% in the COVID-19 vaccine (Original, Wuhan

strain) group, resulting in a difference in seroresponse rates (percentage) of 22.3% (95% CIs: 13.6%, 30.6%).

2. The safety of the of a booster dose of NVX-CoV2601 (Omicron XBB.1.5 subvariant vaccine) was evaluated in participants ≥ 18 years of age who previously received ≥ 3 doses of the Moderna and/or Pfizer/BioNTech prototype monovalent and/or BA.4/5 containing bivalent mRNA COVID- 19 vaccines administered ≥ 90 days prior to study vaccination and in baseline SARS-CoV-2 seropositive COVID-19 vaccine naïve participants ≥ 18 years of age in the US and its territories. Solicited local injection site AEs were reported in 189 (56.9%) participants within 7 days following booster vaccination with NVX-CoV2601, with higher frequencies in participants 18 to 54 years of age (64.2%) than in participants ≥ 55 years of age (48.7%). Pain/tenderness were the most frequent (incidence > 20%) solicited local injection site AEs. Fatigue/malaise, muscle pain, and headache were the most frequent (incidence > 20%) solicited systemic AEs. Unsolicited AEs within 28 days of booster vaccination with NVX-CoV2601 were reported in less than 10% of participants, with most unsolicited AEs being mild or moderate in severity and not related to study vaccine. SAEs were infrequent, occurring in 2 (0.6%) participants, none were related to study vaccine.

   Immunogenicity:
   NVX-CoV2601 induced a superior response in adjusted GMT (ID50) versus NVX-CoV2373 against the Omicron XBB.1.5 subvariant pseudovirus (905.9 vs 156.6, respectively) with a GMTR of 5.8 (95% CI: 4.85, 6.91). The NVX-CoV2601 and historical control NVX-CoV2373 GMFR between baseline to Day 28 was 7.9 (95% CI: 6.8, 9.2) and 1.5 (95% CI: 1.3,1.6), respectively. NVX-CoV2601 induced a non-inferior seroresponse rate (SRR) against the Omicron XBB.1.5 subvariant virus versus the historical control Novavax vaccine NVX-CoV2373 (64.3% vs 7.0%, respectively) at Day 28, with a difference in SRRs of 57.2% (95% CI: 50.5, 63.2).

18. Brief summary of review process of dossier (CTD format, CMC, CDL, SEC, GMP conclusions etc.)

The firm has submitted the New Drugs application through SUGAM online portal system in CTD format (Module-I, II, III, IV & V) for grant of permission to manufacture the product Covid -19 Vaccine, Adjuvanted 2023-24 Formula [SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine, Omicron XBB.1.5 variant] (COVOVAX) under New Drugs & Clinical Trial Rules, 2019, which includes manufacturing, testing, process validation & stability data of drug substance [Real

time & accelerated conditions and drug product [Real time (2^0C-8^0C), accelerated (25 ± 2^0C) and stress conditions (37 ± 2^0C)], Non-clinical data & data of overseas clinical trials.

Based on the documents/information submitted by the firm & review of the CMC (DS & DP) data along with the recommendations of COVID-19 SEC dated 29.04.2024, and comments of CDL, Kasauli on dossiers and three batches test reports from CDL, Kasauli the benefit-risk evaluation of proposed SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine, Omicron XBB.1.5 variant was considered favourable for grant of permission for strain change in the approved COVID-19 vaccine and grant of permission of the COVID-19 Vaccine with local clinical trial waiver for restricted use in emergency situation, subject to various regulatory provisions including conduct of Phase IV study in the country to the applicant, M /s. Serum Institute of India Pvt. Ltd. Pune, Maharashtra India to manufacture SARS-CoV-2 rS Protein (COVID-19) Nanoparticle Vaccine, Omicron XBB.1.5 variant as dispersion for intramuscular administration in single dose (0.5 mL) (5 Doses in 5.0 mL vials) with the shelf life of 12 months when stored at 2ºC to 8ºC for active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals of ≥ 12 to < 18 years of age as primary series of two doses (0.5 mL each) 3 weeks apart & as single precautionary dose in individuals of ≥ 18 years of age, who have received primary series of vaccinations.