CLINICAL UPDATE

Brand Name	Moderna COVID-19 Booster
Generic Name	COVID-19 vaccine, mRNA, cx-024414, LNP-S (Moderna)/PF
Drug Manufacturer	ModernaTX, Inc

Clinical Update

TYPE OF CLINICAL UPDATE

New Strength

FDA APPROVAL DATE

January 31, 2022 - **Emergency Use Authorization Only**

LAUNCH DATE

February 24, 2022

REVIEW DESIGNATION

N/A

TYPE OF REVIEW

N/A

DISPENSING RESTRICTIONS

N/A

Overview

INDICATION(S) FOR USE

Moderna COVID-19 Vaccine is authorized for use under an Emergency Use Authorization (EUA) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 18 years of age and older.

MECHANISMS OF ACTION

The nucleoside-modified mRNA in the Moderna COVID-19 Vaccine is formulated in lipid particles, which enable delivery of the nucleoside-modified mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits an immune response to the S antigen, which protects against COVID-19.

DOSAGE FORM(S) AND STRENGTH(S)

Moderna COVID-19 Vaccine is a suspension for injection.

- Each primary series dose is 0.5 mL.
- The booster dose is 0.25 mL.

DOSE & ADMINISTRATION

For intramuscular injection only.

CLINICAL UPDATE

EFFICACY

- **Immunogenicity of a Booster Dose Following a Moderna COVID-19 Vaccine Primary Series:** Effectiveness of a booster dose of the Moderna COVID-19 Vaccine was based on assessment of neutralizing antibody titers (ID50) against a pseudovirus expressing the SARS-CoV-2 Spike protein from a USA_WA1/2020 isolate carrying the D614G mutation. Immunogenicity analyses compared the ID50 following the booster dose to the ID50 following the primary series.

  Immunogenicity analyses included an assessment of ID50 geometric mean titer (GMT) ratio and difference in seroresponse rates. The analysis of the GMT ratio of ID50 following the booster dose compared to the primary series met the immunobridging criteria for a booster response. Revised: Jan/31/2022 32 Seroresponse for a participant was defined as achieving a ≥4-fold rise in ID50 from baseline (before the booster dose in Study 2 and before the first dose of the primary series in Study 1). The lower limit of the 2-sided 95% CI for the difference in seroresponse rates between Study 1 and Study 2 was -16.7%, which did not meet the immunobridging criterion for a booster response (lower limit of 2-sided 95% CI for the percentage difference of ≥ -10%). These analyses are summarized in Tables 1 and 2.

  Table 1: Neutralizing Antibody Geometric Mean Titers (ID50) Against a Pseudovirus Expressing the SARS-CoV-2 Spike Protein (USA_WA1/2020 isolate carrying the D614G mutation) at 28 Days After a Booster Dose in Study 2 vs 28 Days After Completion of the Primary Series in Study 1, Participants ≥18 Years of Age, Per-Protocol Immunogenicity Set*

Study 2 Booster Dose N[a]=149 GMT[b] (95% CI)	Study 1 Primary Series N[a]=1053 GMT[b] (95% CI)	GMT Ratio (Study 2/Study 1)	Met Success Criteria[c]
1802 (1548, 2099)	1027 (968, 1089)	1.8 (1.5, 2.1)	Lower limit of 95% CI ≥0.67 Criterion: Yes Point Estimate ≥1.0 Criterion: Yes

* Per-Protocol Immunogenicity Set included all subjects who had both baseline (or Study 2 Day 1 for Study 2) and post-vaccination immunogenicity samples, did not have SARS-CoV-2 infection at baseline (or Study 2 Day 1 for Study 2), did not have a major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest (Day 29 for Study 2 and Day 57 for Study 1).

[a] Number of subjects with non-missing data at the corresponding timepoint.

[b] Given the lack of randomization in Study 2, the statistical analysis plan pre-specified an analysis of covariance model for estimating the geometric mean titer that adjusts for differences in age groups (<65 years, ≥65 years).

[c] Immunobridging is declared if the lower limit of the 2-sided 95% CI for the GMR is >0.67 and the point estimate of the GLSM ratio is ≥1.0.

Note: Antibody values < the lower limit of quantitation (LLOQ) are replaced by 0.5 × LLOQ. Values > the upper limit of quantitation (ULOQ) are replaced by the ULOQ if actual values are not available.

GLSM = Geometric least squares mean

GMR = Geometric mean ratio

Table 2: Seroresponse Rates Against a Pseudovirus Expressing the SARS-CoV-2 Spike Protein (USA_WA1/2020 isolate carrying the D614G mutation) at 28 Days Post-Booster Dose in Study 2 and 28 Days After Completion of the Primary Series in Study 1, Participants ≥18 Years of Age, Per-Protocol Immunogenicity Set*

Study 2 Booster Seroresponse[a] N[b]=149 n (%) (95% CI)[c]	Study 1 Primary Series Seroresponse[a] N[b]=1050 n (%) (95% CI)[c]	Difference in Seroresponse Rate (Study 2-Study 1) % (95% CI)[d]	Met Success Criterion[e]
131 (87.9) (81.6, 92.7)	1033 (98.4) (97.4, 99.1)	-10.5 (-16.7, -6.1)	Lower limit of 95% CI ≥-10% Criterion: No

* Per-Protocol Immunogenicity Set included all subjects who had both baseline (or Study 2 Day 1 for Study 2) and post-vaccination immunogenicity samples, did not have SARS-CoV-2 infection at baseline (or Study 2 Day 1 for Study 2), did not have a major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest (Day 29 for Study 2 and Day 57 for Study 1).

[a] Seroresponse is defined as ≥4-fold rise of pseudovirus neutralizing antibody titers (ID50) from baseline (pre-booster dose in Study 2 and pre-Dose 1 in Study 1), where baseline titers < LLOQ are set to LLOQ for the analysis.

[b] Number of subjects with non-missing data at both baseline and the post-baseline timepoint of interest.

[c] 95% CI is calculated using the Clopper-Pearson method.

[d] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

[e] Immunobridging is declared if the lower limit of the 2-sided 95% CI for the percentage difference is > -10%.

An additional descriptive analysis evaluated seroresponse rates using baseline neutralizing antibody titers prior to Dose 1 of the primary series. As shown in Table 3 below, the booster dose seroresponse rate, with seroresponse defined as at least a 4-fold rise relative to the pre-Dose 1 titer, was 100%. The difference in seroresponse rates in this post-hoc analysis was 1.6% (95% CI -0.9, 2.6).

Table 3: Analysis of Seroresponse Rates Against a Pseudovirus Expressing the SARS-CoV2 Spike Protein (USA_WA1/2020 isolate carrying the D614G mutation) at 28 Days PostBooster Dose in Study 2 and 28 Days After Completion of the Primary Series in Study 1, Participants ≥18 Years of Age, Per-Protocol Immunogenicity Set*

Study 2 Booster Seroresponse[a] N[b]=148 n (%) (95% CI)[d]	Study 1 Primary Series Seroresponse[a] N[c]=1050 n (%) (95% CI)[d]	Difference in Seroresponse Rate (After Booster-After Primary Series) % (95% CI)[e]
148 (100) (97.5, 100)	1033 (98.4) (97.4, 99.1)	1.6 (-0.9, 2.6)

* Per-Protocol Immunogenicity Set included all subjects who had non-missing data at baseline (before Dose 1) and 28 days post-booster in Study 2 or 28 days post-Dose 2 in the primary series in Study 1, respectively, did not have SARS-CoV-2 infection at pre-booster in Study 2 or baseline in Study 1, did not have a major protocol deviation that impacted immune response, and had post-injection immunogenicity assessment at timepoint of primary interest.

[a] Seroresponse is defined as ≥4-fold rise of pseudovirus neutralizing antibody titers (ID50) from pre-Dose 1, where baseline titers < LLOQ are set to LLOQ for the analysis.

[b] Number of subjects with non-missing data at baseline (before Dose 1) and 28 days post-booster in Study 2.

[c] Number of subjects with non-missing data at baseline (before Dose 1) and 28 days post-Dose 2 in the primary series in Study 1.

[d] 95% CI is calculated using the Clopper-Pearson method.

[e] 95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

- **Immunogenicity of a Booster Dose Following Primary Vaccination with Another Authorized or Approved COVID-19 Vaccine:**
  Effectiveness of a Moderna COVID-19 Vaccine booster dose (0.25 mL) in individuals who completed primary vaccination with another authorized or approved COVID-19 vaccine (heterologous booster dose) is inferred from immunogenicity data supporting effectiveness of a Moderna COVID-19 Vaccine (0.25 mL) booster dose administered following completion of a Moderna COVID-19 Vaccine primary series and from immunogenicity data from an independent Phase 1/2 open-label clinical trial (NCT04889209) conducted in the United States that evaluated a booster dose (0.5 mL) of the Moderna COVID-19 Vaccine. In this study, adults who had completed primary vaccination with a Moderna COVID-19 Vaccine 2-dose series (N=151), a Janssen COVID-19 Vaccine single dose (N=156), or a Pfizer-BioNTech COVID-19 Vaccine 2- dose series (N=151) at least 12 weeks (range 12 to 20 weeks) prior to enrollment and who reported no history of SARS-CoV-2 infection were randomized 1:1:1 to receive a booster dose of one of three vaccines: Moderna COVID-19 Vaccine, Janssen COVID-19 Vaccine, or PfizerBioNTech COVID-19 Vaccine. Neutralizing antibody titers, as measured by a pseudovirus neutralization assay using a lentivirus expressing the SARS-CoV-2 Spike protein with D614G mutation, were assessed on Day 1 prior to administration of the booster dose and on Day 15 after the booster dose. A booster response to the Moderna COVID-19 Vaccine (0.5 mL) was demonstrated regardless of the vaccine used for primary vaccination.