

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION

MODERNA COVID-19 VACCINE

FULL EUA PRESCRIBING INFORMATION: CONTENTS*

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Table 1: Frequency of Solicited Local and Systemic Reactions Within 7 Days After Each Dose in Participants 18-64 Years (Solicited Safety Set, Dose 1 and Dose 2)

	Moderna COVID-19 Vaccine		Placebo ^a	
	Dose 1 (N=11,405) n (%)	Dose 2 (N=10,358) n (%)	Dose 1 (N=11,406) n (%)	Dose 2 (N=10,321) n (%)
Local Adverse Reactions				
Pain	9,908 (86.9)	9,335 (90.1)	2,179 (19.1)	1,942 (18.8)
Pain, Grade 3 ^b	367 (3.2)	479 (4.6)	23 (0.2)	21 (0.2)
Lymphadenopathy	1,322 (11.6)	1,654 (16.0)	567 (5.0)	444 (4.3)
Lymphadenopathy, Grade 3 ^b	36 (0.3)	45 (0.4)	13 (0.1)	10 (<0.1)
Swelling (hardness)	768 (6.7)	1,309 (12.6)	33 (0.3)	35 (0.3)
Swelling (hardness), Grade 3 ^c	62 (0.5)	176 (1.7)	3 (<0.1)	4 (<0.1)
Erythema (redness)	345 (3.0)	928 (9.0)	46 (0.4)	42 (0.4)
Erythema (redness), Grade 3 ^c	34 (0.3)	206 (2.0)	11 (<0.1)	12 (0.1)
Systemic Adverse Reactions				
Fatigue	4,384 (38.5)	7,002 (67.6)	3,282 (28.8)	2,530 (24.5)
Fatigue, Grade 3 ^d	120	1,099	83	81

	(1.1)	(10.6)	(0.7)	(0.8)
Fatigue, Grade 4 ^e	1 (<0.1)	0 (0)	0 (0)	0 (0)
Headache	4,031 (35.4)	6,500 (62.8)	3,303 (29.0)	2,617 (25.4)
Headache, Grade 3 ^f	219 (1.9)	515 (5.0)	162 (1.4)	124 (1.2)
Myalgia	2,698 (23.7)	6,353 (61.3)	1,626 (14.3)	1,312 (12.7)
Myalgia, Grade 3 ^d	73 (0.6)	1,032 (10.0)	38 (0.3)	39 (0.4)
Arthralgia	1,892 (16.6)	4,685 (45.2)	1,327 (11.6)	1,087 (10.5)
Arthralgia, Grade 3 ^d	47 (0.4)	603 (5.8)	29 (0.3)	36 (0.3)
Arthralgia, Grade 4 ^e	1 (<0.1)	0 (0)	0 (0)	0 (0)
Chills	1,051 (9.2)	5,001 (48.3)	730 (6.4)	611 (5.9)
Chills, Grade 3 ^g	17 (0.1)	151 (1.5)	8 (<0.1)	14 (0.1)
Gastrointestinal Symptoms ^h	1,069 (9.4)	2,209 (21.3)	908 (8.0)	754 (7.3)
Gastrointestinal symptoms, Grade 3 ^{h,i}	6 (<0.1)	8 (<0.1)	8 (<0.1)	8 (<0.1)
Fever	105 (0.9)	1,806 (17.4)	39 (0.3)	38 (0.4)
Fever, Grade 3 ^j	10 (<0.1)	168 (1.6)	1 (<0.1)	1 (<0.1)
Fever, Grade 4 ^k	4 (<0.1)	10 (<0.1)	4 (<0.1)	2 (<0.1)

* 7 days included day of vaccination and the subsequent 6 days.

^a Placebo was a saline solution.

^b Grade 3 pain and lymphadenopathy: Defined as any use of prescription pain reliever; prevents daily activity.

^c Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.

^d Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.

^e Grade 4 fatigue, arthralgia: Defined as requires emergency room visit or hospitalization.

^f Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.

^g Grade 3 chills: Defined as prevents daily activity and requires medical intervention.

^h Gastrointestinal symptoms = nausea, vomiting, diarrhea, and/or abdominal pain.

ⁱ Grade 3 gastrointestinal symptoms: Defined as prevents daily activity, requires outpatient intravenous hydration.

^j Grade 3 fever: Defined as $\geq 39.0 - \leq 40.0^{\circ}\text{C}$ / $\geq 102.1 - \leq 104.0^{\circ}\text{F}$.

^k Grade 4 fever: Defined as $>40.0^{\circ}\text{C}$ / $>104.0^{\circ}\text{F}$.

Table 2: Frequency of Solicited Local and Systemic Reactions Within 7 Days After Each Dose in Participants 65 Years and Older (Solicited Safety Set, Dose 1 and Dose 2)

	Moderna COVID-19 Vaccine		Placebo ^a	
	Dose 1 (N=3,762) n (%)	Dose 2 (N=3,589) n (%)	Dose 1 (N=3,748) n (%)	Dose 2 (N=3,549) n (%)

Local Adverse Reactions				
Pain	2,782 (74.0)	2,990 (83.4)	481 (12.8)	421 (11.9)
Pain, Grade 3 ^b	50 (1.3)	96 (2.7)	32 (0.9)	17 (0.5)
Lymphadenopathy	231 (6.1)	302 (8.4)	155 (4.1)	90 (2.5)
Lymphadenopathy, Grade 3 ^b	12 (0.3)	21 (0.6)	14 (0.4)	8 (0.2)
Swelling (hardness)	166 (4.4)	386 (10.8)	19 (0.5)	13 (0.4)
Swelling (hardness), Grade 3 ^c	20 (0.5)	69 (1.9)	3 (<0.1)	7 (0.2)
Erythema (redness)	86 (2.3)	265 (7.4)	19 (0.5)	13 (0.4)
Erythema (redness), Grade 3 ^c	8 (0.2)	75 (2.1)	2 (<0.1)	3 (<0.1)
Systemic Adverse Reactions				
Fatigue	1,251 (33.3)	2,094 (58.4)	851 (22.7)	695 (19.6)
Fatigue, Grade 3 ^d	30 (0.8)	248 (6.9)	23 (0.6)	20 (0.6)
Headache	921 (24.5)	1,665 (46.4)	724 (19.3)	635 (17.9)
Headache, Grade 3 ^e	52 (1.4)	107 (3.0)	34 (0.9)	32 (0.9)
Myalgia	743 (19.8)	1,683 (46.9)	443 (11.8)	385 (10.8)
Myalgia, Grade 3 ^d	17 (0.5)	201 (5.6)	9 (0.2)	10 (0.3)
Arthralgia	618 (16.4)	1,252 (34.9)	456 (12.2)	381 (10.7)
Arthralgia, Grade 3 ^d	13 (0.3)	122 (3.4)	8 (0.2)	7 (0.2)
Chills	202 (5.4)	1,099 (30.6)	148 (4.0)	144 (4.1)
Chills, Grade 3 ^f	7 (0.2)	27 (0.8)	6 (0.2)	2 (<0.1)
Gastrointestinal symptoms ^g	194 (5.2)	425 (11.8)	166 (4.4)	129 (3.6)
Gastrointestinal symptoms, Grade 3 ^{g,h}	4 (0.1)	10 (0.3)	4 (0.1)	3 (<0.1)
Gastrointestinal symptoms, Grade 4 ^{g,i}	0 (0)	1 (<0.1)	0 (0)	0 (0)
Fever	10 (0.3)	366 (10.2)	7 (0.2)	5 (0.1)
Fever, Grade 3 ^j	1 (<0.1)	18 (0.5)	1 (<0.1)	0 (0)
Fever, Grade 4 ^k	0 (0)	1 (<0.1)	2 (<0.1)	1 (<0.1)

* 7 days included day of vaccination and the subsequent 6 days.

^a Placebo was a saline solution.

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- ^b Grade 3 pain and lymphadenopathy: Defined as any use of prescription pain reliever; prevents daily activity.
- ^c Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.
- ^d Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
- ^e Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.
- ^f Grade 3 chills: Defined as prevents daily activity and requires medical intervention.
- ^g Gastrointestinal symptoms = nausea, vomiting, diarrhea, and/or abdominal pain.
- ^h Grade 3 gastrointestinal symptoms: Defined as prevents daily activity, requires outpatient intravenous hydration.
- ⁱ Grade 4 gastrointestinal symptoms: Defined as requires emergency room visit or hospitalization for hypotensive shock.
- ^j Grade 3 fever: Defined as $\geq 39.0 - \leq 40.0^{\circ}\text{C}$ / $\geq 102.1 - \leq 104.0^{\circ}\text{F}$.
- ^k Grade 4 fever: Defined as $> 40.0^{\circ}\text{C}$ / $> 104.0^{\circ}\text{F}$.

11 USE IN SPECIFIC POPULATIONS

11.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Moderna COVID-19 Vaccine during pregnancy. Women who are vaccinated with Moderna COVID-19 Vaccine during pregnancy are encouraged to enroll in the registry by calling 1-866-MODERNA (1-866-663-3762).

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on Moderna COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy. Therefore, use of Moderna COVID-19 Vaccine is not recommended in pregnant women.

11.2 Lactation

Risk Summary

Data are not available to assess the effects of Moderna COVID-19 Vaccine on the breastfed infant or on milk production/excretion.

11.3 Pediatric Use

Safety and effectiveness have not been assessed in persons less than 18 years of age. Emergency Use Authorization of Moderna COVID-19 Vaccine does not include use in individuals younger than 18 years of age.

11.4 Geriatric Use

Clinical studies of Moderna COVID-19 Vaccine included participants 65 years of age and older receiving vaccine or placebo, and their data contribute to the overall assessment of safety and efficacy. In an ongoing Phase 3 clinical study, 24.8% (n=7,520) of participants were 65 years of age and older and 4.6% (n=1,400) of participants were 75 years of age and older. In an interim analysis, no overall differences in effectiveness were observed between participants 65 years of age and older and participants 18-64 years of age [*see Clinical Trial Results and Supporting*

Data for EUA (18)]. Participants 65 years of age and older reported solicited local and systemic adverse reactions at a lower rate than participants 18-64 years of age. *[see Clinical Trials Experience (6.1)].*

13 DESCRIPTION

Moderna COVID-19 Vaccine is a lipid nanoparticle (LNP) suspension for intramuscular injection comprised of a synthetic messenger ribonucleic acid (mRNA) encoding the pre-fusion stabilized Spike glycoprotein (S) of SARS-CoV-2 virus and four lipids. The synthetic mRNA is manufactured in a cell-free, in vitro transcription reaction and formulated with SM-102 (a proprietary ionizable lipid), PEG2000-DMG, cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC) to form the mRNA/lipid nanoparticles.

Moderna COVID-19 Vaccine is provided as a suspension for intramuscular injection and is white to off-white in appearance. Each 0.5 mL dose contains 100 mcg RNA and a total lipid content of 1.93 mg in tris buffer (0.31 mg tromethamine, 1.18 mg tromethamine hydrochloride), 0.043 mg acetic acid, 0.12 mg sodium acetate, and 43.5 mg sucrose.

Moderna COVID-19 Vaccine does not contain any preservatives, antibiotics, adjuvants, or human- or animal-derived materials. The vial stopper does not contain natural rubber latex.

14 CLINICAL PHARMACOLOGY

14.1 Mechanism of Action

The mRNA in the Moderna COVID-19 Vaccine is encapsulated in lipid nanoparticles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits both neutralizing antibody and cellular immune responses to the S antigen, which may contribute to protection against COVID-19.

18 CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA

A Phase 3 randomized, placebo-controlled, observer-blind clinical trial to evaluate the efficacy, safety, and immunogenicity of the Moderna COVID-19 Vaccine in participants 18 years of age and older is ongoing in the United States (NCT04470427). Randomization was stratified by age and health risk: 18 to <65 years of age without comorbidities (not at risk for progression to severe COVID-19), 18 to <65 years of age with comorbidities (at risk for progression to severe COVID-19), and 65 years of age and older with or without comorbidities. Participants who were immunocompromised and those with a known history of SARS-CoV-2 infection were excluded from the study. Participants with no known history of SARS-CoV-2 infection but with positive laboratory results indicative of infection at study entry were included. The study allowed for the inclusion of participants with stable pre-existing medical conditions, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 3 months before enrollment, as well as participants with stable human immunodeficiency virus (HIV) infection. A total of 30,418 participants were randomized equally to receive 2 doses of the Moderna COVID-19 Vaccine or saline placebo 1 month apart. The efficacy analyses included participants who received their second dose within 21 to 42 days after the first dose. Participants will be followed for efficacy and safety until 24 months after the second dose.

The primary efficacy analysis population (referred to as the Per-Protocol Set), included 27,817 participants who received two doses (at 0 and 1 month) of either Moderna COVID-19 Vaccine (n=13,934) or placebo (n=13,883), and had a negative baseline SARS-CoV-2 status. In the Per-Protocol Set, 47.4% were female, 20% were Hispanic or Latino; 79.4% were white, 9.7% were African American, 4.7% were Asian, and 3.1% other races. The median age of participants was 53 years (range 18-95) and 25.3% of participants were 65 years of age and older. Of the study participants in the Per Protocol Set, 22.3% were at increased risk of severe COVID-19 due to at least one pre-existing medical condition (chronic lung disease, significant cardiac disease, severe obesity, diabetes, liver disease, or HIV infection) regardless of age. There were no notable differences in demographics or pre-existing medical conditions between participants who received Moderna COVID-19 Vaccine or placebo.

Efficacy Against COVID-19

COVID-19 was defined based on the following criteria: The participant must have experienced at least two of the following systemic symptoms: fever ($\geq 38^{\circ}\text{C}$), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s); or the participant must have experienced at least one of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, or clinical or radiographical evidence of pneumonia; and the participant must have at least one NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS-CoV-2 by RT-PCR. COVID-19 cases were adjudicated by a Clinical Adjudication Committee.

At the time of the interim analysis, the median length of follow up for efficacy for participants in the study was 7 weeks post Dose 2. There were 5 COVID-19 cases in the Moderna COVID-19 Vaccine group and 90 cases in the placebo group, with a vaccine efficacy of 94.5% (95% confidence interval of 86.5% to 97.8%).

Table 3: Interim Primary Efficacy Analysis: COVID-19* in Participants 18 Years of Age and Older Starting 14 Days After Dose 2 per Adjudication Committee Assessments – Per-Protocol Set

Moderna COVID-19 Vaccine			Placebo			% Vaccine Efficacy (95% CI) [†]
Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	
13,934	5	1.840	13,883	90	33.365	94.5 (86.5, 97.8) (p<0.0001) [‡]

* COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least two systemic symptoms or one respiratory symptom. Cases starting 14 days after Dose 2.

[†] VE and 95% CI from the stratified Cox proportional hazard model

[‡] The one-sided p-value is <0.0001 from the stratified Cox proportional hazard model to test the null hypothesis of $\text{VE} \leq 30\%$, achieving the pre-specified efficacy boundary: the one-sided nominal alpha of 0.0049 based on 95 cases using the Lan-DeMets O'Brien-Fleming spending function.

The subgroup analyses of vaccine efficacy are presented in [Table 3](#).

Table 4: Interim Subgroup Analyses of Vaccine Efficacy: COVID-19* Cases Starting 14 Days After Dose 2 per Adjudication Committee Assessments – Per- Protocol Set

Subgroup	Moderna COVID-19 Vaccine			Placebo			% Vaccine Efficacy (95% CI)*
	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	
18 to <65	10,407	5	2.504	10,384	75	37.788	93.4 (83.7, 97.3)
≥65	3,527	0	--	3,499	15	21.046	100

* COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least two systemic symptoms or one respiratory symptom. Cases starting 14 days after Dose 2.

† VE and 95% CI from the stratified Cox proportional hazard model

Severe COVID-19 was defined based on confirmed COVID-19 as per the primary efficacy endpoint case definition, plus any of the following: Clinical signs indicative of severe systemic illness, respiratory rate ≥ 30 per minute, heart rate ≥ 125 beats per minute, SpO₂ $\leq 93\%$ on room air at sea level or PaO₂/FIO₂ < 300 mm Hg; or respiratory failure or ARDS, (defined as needing high-flow oxygen, non-invasive or mechanical ventilation, or ECMO), evidence of shock (systolic blood pressure < 90 mmHg, diastolic BP < 60 mmHg or requiring vasopressors); or significant acute renal, hepatic, or neurologic dysfunction; or admission to an intensive care unit or death.

Among all participants in the Per-Protocol Set interim analysis, no cases of severe COVID-19 were reported in the Moderna COVID-19 Vaccine group compared with 11 cases reported in the placebo group (incidence rate 4.072 per 1,000 person-years).

19 HOW SUPPLIED/STORAGE AND HANDLING

Moderna COVID-19 Vaccine is supplied as a multiple-dose vial containing 10 doses of 0.5 mL each.

Each carton of Moderna COVID-19 Vaccine contains 10 multiple-dose vials (NDC 80777-273-99).

Store frozen between -25° to -15°C (-13° to 5°F). Store in the original carton to protect from light. Do not store on dry ice or below -40°C (-40°F).

Vials can be stored refrigerated between 2° to 8°C (36° to 46°F) for up to 30 days prior to first use. Do not refreeze.

Unopened vials may be stored between 8° to 25°C (46° to 77°F) for up to 12 hours. Do not refreeze.

After the first dose has been withdrawn, the vial should be held between 2° to 25°C (36° to 77°F). Discard vial after 6 hours. Do not refreeze.

20 PATIENT COUNSELING INFORMATION

Advise the recipient or caregiver to read the Fact Sheet for Recipients and Caregivers.

21 CONTACT INFORMATION

If you have questions, please contact: Moderna
1-866-MODERNA (1-866-663-3762)
medinfo@modernatx.com

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