PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

COVID-19 Vaccine Moderna

mRNA-1273 SARS-CoV-2 vaccine

Dispersion for intramuscular injection

Multidose Vial, 100 mcg / 0.5mL (per dose)

(contains 10 doses of 0.5 mL)

Active Immunizing Agent

HEALTH CANADA HAS AUTHORIZED THE SALE OF THIS COVID-19 Vaccine UNDER AN INTERIM ORDER

COVID-19 Vaccine Moderna is indicated for:

Active immunization against coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus in individuals 18 years of age and older.

The use of COVID-19 Vaccine Moderna is permitted under an interim authorization delivered in accordance with section 5 of the COVID-19 Interim order (IO)*. Patients should be advised of the nature of the authorization. The interim authorization is associated with Terms and Conditions that need to be met by the Market Authorization Holder to ascertain the continued quality, safety and efficacy of the product. For further information on authorization under this pathway, please refer to Health Canada's IO Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19.

* https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/interim-order-import-sale-advertising-drugs.html#a2.8

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

COVID-19 Vaccine Moderna (mRNA-1273 SARS-CoV-2 vaccine) is indicated for active immunization against coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus in individuals 18 years of age and older.

1.1 Pediatrics

The safety and efficacy of COVID-19 Vaccine Moderna in individuals under 18 years of age has not yet been established. (See ADVERSE REACTIONS, and CLINICAL TRIALS sections)

1.2 Geriatrics

Clinical studies of COVID-19 Vaccine Moderna include participants 65 years of age and older and their data contributes to the overall assessment of safety and efficacy (See ADVERSE REACTIONS and CLINICAL TRIALS sections).

2 CONTRAINDICATIONS

COVID-19 Vaccine Moderna is contraindicated in individuals who are hypersensitive to the active ingredient or to any ingredients in the formulation, including any non-medicinal ingredient, or component of the container. (For a complete listing, see DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING sections).

3 SERIOUS WARNING AND PRECAUTIONS

At the time of authorization, there are no known serious warnings or precautions associated with this product.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

COVID-19 Vaccine Moderna is a dispersion for intramuscular injection that should be administered by a trained healthcare worker. COVID-19 Vaccine Moderna is a two-dose regimen. The second dose should be administered 4 weeks after the first dose.

4.2 Recommended Dose and Dosage Adjustment

COVID-19 Vaccine Moderna should be administered intramuscularly, as two 0.5 mL doses, 4 weeks apart.

There are no data available on the interchangeability of COVID-19 Vaccine Moderna with other COVID-19 vaccines to complete the vaccination series. Individuals who have received one dose of COVID-19 Vaccine Moderna should receive a second dose of COVID-19 Vaccine Moderna to complete the vaccination series.

4.3 Reconstitution

COVID-19 Vaccine Moderna must not be reconstituted, mixed with other medicinal products, or diluted.

4.4 Administration

Use aseptic technique for preparation and administration.

Preparation

Thaw each vial before use:

- Thaw in refrigerated conditions between 2°C to 8°C for 2 hours and 30 minutes. Let each vial stand at room temperature for 15 minutes before administering.
- Alternatively, thaw at room temperature between 15°C to 25°C for 1 hour.
- Do not re-freeze vials after thawing.

Swirl the vial gently after thawing and between each withdrawal. Do not shake.

Administration

COVID-19 Vaccine Moderna is a white to off-white dispersion. It may contain white or translucent product-related particulates. Inspect COVID-19 Vaccine Moderna vials visually for foreign particulate matter and/or discoloration prior to administration. If either of these conditions exists, the vaccine should not be administered.

COVID-19 Vaccine Moderna should be administered by the intramuscular (IM) route only. Do not inject the vaccine intravascularly, subcutaneously or intradermally. The preferred site is the deltoid muscle of the upper arm. A needle length of ≥1 inch should be used as needles <1 inch may be of insufficient length to penetrate muscle tissue in some adults.

Using aseptic technique, cleanse the vial stopper with a single-use antiseptic swab.

Withdraw each 0.5 mL dose of vaccine from the vial using a new sterile needle and syringe for each injection. The dose in the syringe should be used as soon as feasible and no later than 6 hours after the vial was first entered (needle-punctured).

COVID-19 Vaccine Moderna is preservative free. Once the vial has been entered, it should be discarded after 6 hours. Do not refreeze. Any unused vaccine or waste material should be disposed of in accordance with local requirements.

5 OVERDOSAGE

In the case of a suspected vaccine overdose, monitoring of vital functions and symptomatic treatment are recommended. Contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1: Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intramuscular injection	Dispersion, (0.20 mg /mL), mRNA, encoding the pre fusion stabilized Spike glycoprotein of 2019 novel Coronavirus (SARS-CoV-2) Multidose vial (5 mL, containing 10 doses of 0.5 mL)	• 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC) • Acetic acid • Cholesterol • Lipid SM-102 • PEG2000 DMG 1,2-dimyristoyl-rac-glycerol,methoxy-polyethyleneglycol • Sodium acetate trihydrate • Sucrose • Trometamol • Trometamol hydrochloride • Water for injection

COVID-19 Vaccine Moderna is provided as a white to off-white sterile dispersion for intramuscular injection. COVID-19 Vaccine Moderna contains a lipid nanoparticle (LNP) comprised of a messenger ribonucleic acid (mRNA) encoding the pre-fusion stabilized Spike glycoprotein of SARS-CoV-2 virus and four lipids, formulated with the non-medicinal ingredients listed in Table 1. COVID-19 Vaccine Moderna does not contain any preservatives, antibiotics, adjuvants, or human- or animal-derived materials.

COVID-19 Vaccine Moderna is supplied in a multi-dose 10R type I glass vial (each of 5 mL) with a 20 mm Fluro Tec-coated chlorobutyl elastomer stopper, 20 mm flip-off aluminum seal. The vial stopper does not contain natural rubber latex. Vials are packaged in a secondary carton containing a total of ten (10) mRNA-1273 vaccine vials per carton.

To help ensure the traceability of vaccines for patient immunization record-keeping as well as safety monitoring, health professionals should record the time and date of administration, quantity of administered dose (if applicable), anatomical site and route of administration, brand name and generic name of the vaccine, the product lot number and expiry date.

7 WARNINGS AND PRECAUTIONS

The clinical data available for COVID-19 Vaccine Moderna are derived from the COVE Phase 3 study and Phase 1 and Phase 2 studies. Serious and unexpected adverse events may occur that have not been previously reported with COVID-19 Vaccine Moderna use.

As with any vaccine, vaccination with COVID-19 Vaccine Moderna may not protect all recipients.

Individuals may not be optimally protected until after receiving the second dose of the vaccine.

Hypersensitivity and Anaphylaxis

Anaphylaxis has been reported. As with all vaccines, appropriate medical treatment, training for immunizers and supervision after immunization should always be readily available in case of a rare anaphylactic event following the administration of this vaccine. Vaccine recipients should be kept

under observation for at least 15 minutes after immunization; 30 minutes is a preferred interval when there is a specific concern about a possible vaccine reaction. A second dose of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of COVID-19 Vaccine Moderna.

Acute illness

Consideration should be given to postponing immunization in persons with severe febrile illness or severe acute infection. Persons with moderate or severe acute illness should be vaccinated as soon as the acute illness has improved.

Hematologic-Bleeding

As with other intramuscular injections, COVID-19 Vaccine Moderna should be given with caution in individuals with bleeding disorders, such as haemophilia, or individuals currently on anticoagulant therapy, to avoid the risk of haematoma following the injection, and when the potential benefit clearly outweighs the risk of administration.

Immune

Immunocompromised persons, including individuals receiving immunosuppressant therapy, may have a diminished immune response to the vaccine.

Syncope

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. Procedures should be in place to prevent injury from fainting and manage syncopal reactions.

7.1 Special Populations

7.1.1 Pregnant Women

The safety and efficacy of COVID-19 Vaccine Moderna in pregnant women have not yet been established.
There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to COVID-19 Vaccine Moderna during pregnancy. Women who are vaccinated with COVID-19 Vaccine Moderna during pregnancy are encouraged to enroll in the registry by calling 1-866-MODERNA (1-866-663- 3762).

7.1.2 Breast-feeding

It is unknown if COVID-19 Vaccine Moderna is excreted in human milk. A risk to the newborns/ infants cannot be excluded. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for immunization against COVID-19.

7.1.3 Pediatrics

The safety and efficacy of COVID-19 Vaccine Moderna in children have not yet been established.

7.1.4 Geriatrics

Clinical studies of COVID-19 Vaccine Moderna include participants 65 years of age and older and their data contributes to the overall assessment of safety and efficacy (See ADVERSE REACTIONS and CLINICAL TRIALS sections).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The safety profile presented below is based on data generated from an ongoing Phase 3 placebo-controlled clinical study on subjects ≥ 18 years of age.

Solicited adverse reactions were reported more frequently among vaccine subjects than placebo subjects. The most frequently reported adverse reactions after any dose were pain at the injection site (92.0%), fatigue (70.0%), headache (64.7%), myalgia (61.5%) and chills (45.4%). The majority of local and systemic adverse reactions had a median duration of 1 to 3 days.

Overall, there was a higher reported rate of solicited adverse reactions in younger age groups; the incidence of lymphadenopathy (axillary swelling/tenderness), fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting, fever was higher in adults 18 to 64 years of age than in those 65 years of age and above. Solicited adverse reactions were also more frequent after the second dose, compared to the first one, including grade 3 local and systemic adverse reactions (see Table 2, Table 3, Table 4 and Table 5 respectively).

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another vaccine. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse vaccine reactions in real-world use.

The safety profile presented below is based on data generated in an ongoing Phase 3, placebo-controlled clinical study on subjects ≥ 18 years of age in which pre-specified cohorts of subjects who were either ≥65 years of age or 18 to 64 years of age with comorbid medical conditions were included. At the time of the analysis, the safety analysis set included a total of 30,351 subjects who received at least one dose of COVID-19 Vaccine Moderna (n=15,181) or placebo (n=15,170). Subjects were followed for a median of 92 days from first injection and 63 days from second injection.

Solicited adverse reaction data were collected from Day 1 to Day 7 and reported by participants in an electronic diary (e-Diary) after each dose and on electronic case report forms. Reported solicited local and systemic adverse reactions are presented in Table 2, Table 3, Table 4 and Table 5 respectively.

Table 2: Solicited Local Adverse Reactions Within 7 Days After First and Second Injection by Grade- Participants 18-64 Years of Age (Safety Analysis Set*)

Solicited local AR	Dose 1		Dose 2	
	Vaccine Group n (%) N=11406	Placebo Group n (%) N=11407	Vaccine Group n (%) N=10985	Placebo Group n (%) N=10918
Pain				
Any grade	9908 (86.9)	2177 (19.1)	9873 (89.9)	2040 (18.7)
Grade 3 or 4[a]	366 (3.2)	23 (0.2)	506 (4.6)	22 (0.2)
Erythema				
Any grade	344 (3.0)	47 (0.4)	982 (8.9)	43 (0.4)
Grade 3 or 4[b]	34 (0.3)	11 (<0.1)	210 (1.9)	12 (0.1)
Swelling/Induration				
Any grade	767 (6.7)	34 (0.3)	1389 (12.6)	36 (0.3)
Grade 3 or 4[b]	62 (0.5)	3 (<0.1)	182 (1.7)	4 (<0.1)
Axillary swelling/ Tenderness				
Any grade	1322 (11.6)	567 (5.0)	1775 (16.2)	470 (4.3)
Grade 3 or 4	37 (0.3)	13 (0.1)	46 (0.4)	11 (0.1)

*Safety Analyses Set: all randomized participants who received ≥1 vaccine or control dose.
Note: Adverse reaction data were collected from Day 1 to Day 7 after each dose on the electronic diary (e-Diary) by participants and those collected on the eCRF indicated as solicited adverse reactions.
n= # of participants with specified reaction, percentages are based on n/N
N= number of exposed subjects who submitted any data for the event.
[a] Pain - Grade 3: any use of Rx pain reliever/prevents daily activity; Grade 4: requires E.R. visit or hospitalization
[b] Erythema and Swelling/Induration - Grade 3: >100mm/>10cm; Grade 4: necrosis/exfoliative dermatitis
[c] Axillary Swelling/Tenderness collected as solicited local adverse reaction (i.e., lymphadenopathy: localized axillary swelling or tenderness ipsilateral to the vaccination arm) - Grade 3: any use of Rx pain reliever/prevents daily activity; Grade 4: requires E.R. visit or hospitalization.

Table 3: Solicited Local Adverse Reactions Within 7 Days After First and Second Injection by Grade- Participants 65 Years of Age and Older (Safety Analysis Set*)

Solicited local AR	Dose 1		Dose 2	
	Vaccine Group n (%) N=3762	Placebo Group n (%) N=3748	Vaccine Group n (%) N=3692	Placebo Group n (%) N=3648
Pain				
Any grade	2782 (74.0)	481 (12.8)	3070 (83.2)	437 (12.0)
Grade 3 or 4[a]	50 (1.3)	32 (0.9)	98 (2.7)	18 (0.5)
Erythema				

Solicited local AR	Dose 1		Dose 2	
	Vaccine Group n (%) N=3762	Placebo Group n (%) N=3748	Vaccine Group n (%) N=3692	Placebo Group n (%) N=3648
Any grade	86 (2.3)	20 (0.5)	275 (7.5)	13 (0.4)
Grade 3 or 4[b]	8 (0.2)	2 (<0.1)	77 (2.1)	3 (<0.1)
Swelling/Induration				
Any grade	165 (4.4)	18 (0.5)	400 (10.8)	13 (0.4)
Grade 3 or 4[b]	20 (0.5)	3 (<0.1)	72 (2.0)	7 (0.2)
Axillary swelling/ Tenderness				
Any grade	231 (6.1)	155 (4.1)	315 (8.5)	97 (2.7)
Grade 3 or 4	12 (0.3)	14 (0.4)	21 (0.6)	8 (0.2)

*Safety Analyses Set: all randomized participants who received ≥1 vaccine or control dose.
Note: Adverse reaction data were collected from Day 1 to Day 7 after each dose on the electronic diary (e-Diary) by participants and those collected on the eCRF indicated as solicited adverse reactions.
n= # of participants with specified reaction, percentages are based on n/N
N= number of exposed subjects who submitted any data for the event.
[a] Pain - Grade 3: any use of Rx pain reliever/prevents daily activity; Grade 4: requires E.R. visit or hospitalization
[b] Erythema and Swelling/Induration - Grade 3: >100mm/>10cm; Grade 4: necrosis/exfoliative dermatitis
[c] Axillary Swelling/Tenderness collected as solicited local adverse reaction (i.e., lymphadenopathy: localized axillary swelling or tenderness ipsilateral to the vaccination arm) - Grade 3: any use of Rx pain reliever/prevents daily activity; Grade 4: requires E.R. visit or hospitalization.

Table 4: Solicited Systemic Adverse Reactions Within 7 Days After First and Second Injection by Grade -Participants 18-64 Years of Age (Safety Analysis Set*)

Solicited Systemic AR	Dose 1		Dose 2	
	Vaccine Group n (%) N=11406	Placebo Group n (%) N=11407	Vaccine Group n (%) N=10985	Placebo Group n (%) N=10918
Fatigue				
Any grade	4,384 (38.4)	3,282 (28.8)	7,430 (67.6)	2,687 (24.6)
Grade 3[a]	120 (1.1)	83 (0.7)	1,174 (10.7)	86 (0.8)
Grade 4[b]	1 (<0.1)	0 (0)	0 (0)	0 (0)
Headache				
Any grade	4,030 (35.3)	3,304 (29.0)	6,898 (62.8)	2,760 (25.3)
Grade 3[c]	219 (1.9)	162 (1.4)	553 (5.0)	129 (1.2)

Solicited Systemic AR	Dose 1		Dose 2	
	Vaccine Group n (%) N=11406	**Placebo Group** n (%) N=11407	**Vaccine Group** n (%) N=10985	**Placebo Group** n (%) N=10918
Myalgia				
Any grade	2,699 (23.7)	1,628 (14.3)	6,769 (61.6)	1,411 (12.9)
Grade 3[a]	73 (0.6)	38 (0.3)	1,113 (10.1)	42 (0.4)
Arthralgia				
Any grade	1,893 (16.6)	1,327 (11.6)	4,993 (45.5)	1,172 (10.7)
Grade 3[a]	47 (0.4)	29 (0.3)	647 (5.9)	37 (0.3)
Grade 4[b]	1 (<0.1)	0 (0)	0 (0)	0 (0)
Chills				
Any grade	1,051 (9.2)	730 (6.4)	5,341 (48.6)	658 (6.0)
Grade 3[d]	17 (0.1)	8 (<0.1)	164 (1.5)	15 (0.1)
Nausea/vomiting				
Any grade	1,068 (9.4)	908 (8.0)	2,348 (21.4)	801 (7.3)
Grade 3[e]	6 (<0.1)	8 (<0.1)	10 (<0.1)	8 (<0.1)
Fever				
Any grade	105 (0.9)	37 (0.3)	1,908 (17.4)	39 (0.4)
Grade 3[f]	10 (<0.1)	1 (<0.1)	184 (1.7)	2 (<0.1)
Grade 4[g]	4 (<0.1)	4 (<0.1)	12 (0.1)	2 (<0.1)
Use of antipyretic or pain medication	2,656 (23.3)	1,523 (13.4)	6,292 (57.3)	1,248 (11.4)

*Safety Analyses Set: all randomized participants who received ≥1 vaccine or control dose.
Note: Adverse reaction data were collected from Day 1 to Day 7 after each dose on the electronic diary (e-Diary) by participants and those collected on the eCRF indicated as solicited adverse reactions.
n= # of participants with specified reaction, percentages are based on n/N
N= number of exposed subjects who submitted any data for the event.
[a] Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
[b] Grade 4 fatigue, arthralgia: Defined as requires emergency room visit or hospitalization.
[c] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.
[d] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.
[e] Grade 3 nausea/vomiting: Defined as prevents daily activity, requires outpatient intravenous hydration.
[h] Grade 3 fever: Defined as ≥39.0 – ≤40.0°C / ≥102.1 – ≤104.0°F.
[i] Grade 4 fever: Defined as >40.0°C / >104.0°F.

Table 5: Solicited Systemic Adverse Reactions Within 7 Days After First and Second Injection by Grade -Participants 65 Years of Age and Older (Safety Analysis Set*)

Solicited Systemic AR	Dose 1		Dose 2	
	Vaccine Group n (%) N=3762	**Placebo Group** n (%) N=3748	**Vaccine Group** n (%) N=3692	**Placebo Group** n (%) N=3648
Fatigue				
Any grade	1251 (33.3)	851 (22.7)	2152 (58.3)	716 (19.6)
Grade 3[a]	30 (0.8)	22 (0.6)	254 (6.9)	20 (0.5)
Headache				
Any grade	921 (24.5)	723 (19.3)	1704 (46.2)	650 (17.8)
Grade 3[b]	52 (1.4)	34 (0.9)	106 (2.9)	33 (0.9)
Myalgia				
Any grade	742 (19.7)	443 (11.8)	1739 (47.1)	398 (10.9)
Grade 3[a]	17 (0.5)	9 (0.2)	205 (5.6)	10 (0.3)
Arthralgia				
Any grade	618 (16.4)	456 (12.2)	1291 (35.0)	397 (10.9)
Grade 3[a]	13 (0.3)	8 (0.2)	123 (3.3)	7 (0.2)
Chills				
Any grade	202 (5.4)	148 (4.0)	1141 (30.9)	151 (4.1)
Grade 3[c]	7 (0.2)	6 (0.2)	27 (0.7)	2 (<0.1)
Nausea/vomiting				
Any grade	194 (5.2)	166 (4.4)	437 (11.8)	133 (3.6)
Grade 3[d]	4 (0.1)	4 (0.1)	10 (0.3)	3 (<0.1)
Grade 4[e]	0 (0)	0 (0)	1 (<0.1)	0 (0)
Fever				
Any grade	10 (0.3)	7 (0.2)	370 (10.0)	4 (0.1)
Grade 3[f]	1 (<0.1)	1 (<0.1)	18 (0.5)	0 (0)
Grade 4[g]	0 (0)	2 (<0.1)	1 (<0.1)	1 (<0.1)
Use of antipyretic or pain medication	673 (17.9)	477 (12.7)	1546 (41.9)	329 (9.0)

*Safety Analyses Set: all randomized participants who received ≥1 vaccine or control dose.
Note: Adverse reaction data were collected from Day 1 to Day 7 after each dose on the electronic diary (e-Diary) by participants and those collected on the eCRF indicated as solicited adverse reactions.
n= # of participants with specified reaction, percentages are based on n/N
N= number of exposed subjects who submitted any data for the event.
[a] Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.
[b] Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.
[c] Grade 3 chills: Defined as prevents daily activity and requires medical intervention.
[d] Grade 3 Nausea/vomiting: Defined as prevents daily activity, requires outpatient intravenous hydration.
[e] Grade 4 Nausea/vomiting: Defined as requires emergency room visit or hospitalization for hypotensive shock.
[f] Grade 3 fever: Defined as ≥39.0 – ≤40.0°C / ≥102.1 – ≤104.0°F.
[g] Grade 4 fever: Defined as >40.0°C / >104.0°F.

Unsolicited Adverse Events

Serious Adverse Events

Serious adverse events were reported in 0.6% of participants who received mRNA-1273 and 0.6% of participants who received a placebo, from the first dose until 28 days following the last vaccination. Serious adverse events were reported in 1% of participants who received mRNA-1273 and 1% of participants who received a placebo, from the first dose until the last observation.

There were no other notable patterns or numerical imbalances between treatment groups for specific categories of adverse events (including other neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship to COVID-19 Vaccine Moderna.

Three serious adverse events were likely related to the mRNA-1273 vaccine: two cases of facial swelling occurring within 7 days of receiving dose 2, in female patients aged 46 and 51; one case of nausea and vomiting with headaches and fever occurring within 7 days after dose 2 and requiring in-hospital treatment in a 61 y.o. female, with past medical history of headaches with nausea and vomiting requiring hospitalization.

No deaths related to the vaccine were reported in the study.

Non-serious Adverse Events

In the Phase 3 study, unsolicited adverse events occurring within 28 days after each vaccination were reported by 23.9% of subjects who received mRNA-1273, and 21.6% of subjects who received the placebo. These adverse events were predominantly solicited adverse reactions occurring outside of the conventional 7-day monitoring period after the injection (injection site pain, fatigue, headaches, myalgia, etc.). Unsolicited adverse events that occurred in ≥ 1% of study participants who received mRNA-1273 and at a rate at least 1.5-fold higher rate than placebo, were lymphadenopathy related events (1.1% of versus 0.6%). All of the lymphadenopathy events are similar to the axillary swelling/tenderness in the injected arm reported as solicited adverse reactions. Hypersensitivity events were reported in 1.5% of the mRNA-1273 group compared to 1.1% of the placebo group, but this imbalance was mostly due to injection site rash and injection site erythema/swelling occurring more frequently in the mRNA-1273 group. There were no other notable patterns or numerical imbalances between treatment groups for specific categories of non-serious adverse events (including neurologic,

musculoskeletal or inflammatory events) that would suggest a causal relationship to COVID-19 Vaccine Moderna.

8.3 Post-Market Adverse Reactions

Anaphylaxis has been reported following COVID-19 Vaccine Moderna administration.

9 DRUG INTERACTIONS

No interaction studies have been performed.

Do not mix COVID-19 Vaccine Moderna with other vaccines/products in the same syringe.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

COVID-19 Vaccine Moderna encodes for the pre-fusion stabilized Spike protein of SARS-CoV-2. After intramuscular injection, cells take up the lipid nanoparticle, effectively delivering the mRNA sequence into cells for expression of the SARS-CoV-2 S antigen. The vaccine induces both neutralizing antibody and cellular immune responses to the spike (S) antigen, which may contribute to protection against COVID-19 disease.

11 STORAGE, STABILITY AND DISPOSAL

Storage Prior to Use

As Displayed on the Vial Labels and Cartons

The COVID-19 Vaccine Moderna multidose vials are stored frozen between -25º to -15ºC (-13º to 5ºF). Store in the original carton to protect from light.

Additional Storage Information Not Displayed on the Vial Labels and Cartons

Do not store on dry ice or below -40ºC (-40ºF).

Vials can be stored refrigerated between 2° to 8°C (36° to 46°F) for up to 30 days prior to first use.

Unpunctured vials may be stored between 8° to 25°C (46° to 77°F) for up to 12 hours.

Do not refreeze once thawed.

Thawing Vials Prior To Use

The COVID-19 Vaccine Moderna multidose vial contains a frozen dispersion that does not contain a preservative and must be thawed prior to administration.

Remove the required number of vial(s) from storage and thaw each vial before use.
Thaw in refrigerated conditions between 2° to 8°C (36° to 46°F) for 2 hours and 30 minutes. After thawing, let vial stand at room temperature for 15 minutes before administering.

Alternatively, thaw at room temperature between 15° to 25°C (59° to 77°F) for 1 hour.

After thawing, do not refreeze.

Punctured vials
COVID-19 Vaccine Moderna is preservative-free. Once the vial has been entered (needle-punctured), it can be stored at room temperature or refrigerated, but must be discarded after 6 hours. Do not refreeze.

12 SPECIAL HANDLING INSTRUCTIONS

COVID-19 Vaccine Moderna must not be mixed with other medicinal products or diluted. Any unused vaccine or waste material should be disposed of in accordance with local requirements.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: mRNA-1273 SARS-CoV-2 vaccine

Chemical name: mRNA-1273 LS (Large Scale) Lipid Nanoparticle (LNP)

Product Characteristics:

COVID-19 Vaccine Moderna is an mRNA-lipid complex [lipid nanoparticle (LNP)] dispersion that contains an mRNA (CX-024414) that encodes for the pre-fusion stabilized Spike glycoprotein of 2019-novel Coronavirus (SARS-CoV-2) and four lipids which act as protectants and carriers of the mRNA. The four lipids are: SM-102 (a custom-manufactured, ionizable lipid); PEG2000-DMG (1,2-dimyristoyl-rac-glycerol,methoxy-polyethyleneglycol); 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC) and cholesterol.

COVID-19 Vaccine Moderna is supplied as a multidose liquid ready-to-use dispersion at 0.20 mg/mL for intramuscular administration. COVID-19 Vaccine Moderna is in a 10R clear Type 1 glass vial with a rubber serum stopper and an aluminum seal with flip-off plastic cap. Each vial contains 1.26 mg of CX-024414 mRNA and 24.38 mg of SM-102 LNP as a white to off-white dispersion in preservative-free diluent buffer at pH 7.5. There are 10 doses per vial.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

The safety and efficacy of mRNA-1273 COVID-19 Vaccine were evaluated in a Phase 3 randomized, placebo-controlled, multicentre study in participants 18 years of age and older. A total of 30,351 (15,181 in the mRNA-1273 COVID-19 Vaccine group and N=15,170 in the placebo group) participants were randomized equally to receive 2 doses of mRNA-1273 COVID-19 Vaccine or placebo separated by 28 days. Randomization was stratified by age and risk of severe COVID-19 as follows: ≥ 65 years old, < 65 years old and at increased risk for the complications of COVID-19, and < 65 years old and not at increased risk for the complications of COVID-19.

Pregnant or breastfeeding women and individuals with known history of SARS-CoV-2 infection, immunosuppressive or immunodeficient state, asplenia or recurrent severe infections were excluded from the study. The primary efficacy was symptomatic* COVID-19 infection confirmed by Polymerase Chain Reaction (PCR) and by a clinical adjudication committee. The population for the analysis of the primary efficacy endpoint included participants who did not have evidence of prior infection with SARS-CoV-2 through 14 days after the second dose. Participants are planned to be followed for up to 24 months for assessments of safety and efficacy against COVID-19 disease.

* Symptomatic COVID-19 case definition: At least two of the following systemic symptoms: fever (≥38ºC), 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.

Table 6: Demographic Characteristics – Subjects Without Evidence of Infection Prior to 14 Days After Dose 2 – Evaluable Efficacy Population

	Vaccine Group (N=14134) n (%)	Placebo Group (N= 14073) n (%)	Total (N=28207) n (%)
Sex			
Female	6768 (47.9)	6611 (47.0)	13379 (47.4)
Male	7366 (52.1)	7462 (53.0)	14828 (52.6)
Age (years)			
Mean (SD)	51.6 (15.44)	51.6 (15.54)	51.6 (15.49)
Median	53.0	52.0	53.0
Min, max	18, 95	18, 95	18, 95
Age – Subgroups (years)			
18 to <65	10551 (74.6)	10521 (74.8)	21072 (74.7)
65 and older	3583 (25.4)	3552 (25.2)	7135 (25.3)
Race			
American Indian or Alaska Native	108 (0.8)	111 (0.8)	219 (0.8)
Asian	620 (4.4)	689 (4.9)	1309 (4.6)
Black or African American	1385 (9.8)	1349 (9.6)	2734 (9.7)
Native Hawaiian or Other Pacific Islander	35 (0.2)	31 (0.2)	66 (0.2)
White	11253 (79.6)	11174 (79.4)	22427 (79.5)
Other	299 (2.1)	295 (2.1)	594 (2.1)
Ethnicity			
Hispanic or Latino	2789 (19.7)	2780 (19.8)	5569 (19.7)
Not Hispanic or Latino	11212 (79.3)	11165 (79.3)	22377 (79.3)
Race and Ethnicity			
Non-Hispanic White	9023 (63.8)	8916 (63.4)	17939 (63.6)
Communities of color	5088 (36.0)	5132 (36.5)	10220 (36.2)
Occupational Risk*	11586 (82.0)	11590 (82.4)	23176 (82.2)
Healthcare worker	3593 (25.4)	3581 (25.4)	7174 (25.4)
High Risk Condition**			
One high risk condition present	2616 (18.5)	2591 (18.4)	5207 (18.5)
Two or more high risk conditions present	590 (4.2)	576 (4.1)	1166 (4.1)
No high risk condition	10928 (77.3)	10906 (77.5)	21834 (77.4)
Age and Health Risk for Severe COVID-19***			
18 to <65 years and not at risk	8189 (57.9)	8200 (58.3)	16389 (58.1)
18 to <65 years and at risk	2367 (16.7)	2324 (16.5)	4691 (16.6)
≥ 65 years	3578 (25.3)	3549 (25.2)	7127 (25.3)

* Occupational risk includes: Healthcare Workers; Emergency Response; Retail/Restaurant Operations; Manufacturing and Production; Operations, Warehouse Shipping and Fulfillment centers, Transportation and Delivery Services, Border Protection and Military Personnel Personal care and in-home services; Hospitality and Tourism Workers, Pastoral; Social or Public Health Workers; and Educators and Students.

** High risk for severe COVID-19 is defined as patients who meet at least one of the following criteria (protocol-defined):

- Chronic lung disease (e.g., emphysema and chronic bronchitis, idiopathic pulmonary fibrosis, and cystic fibrosis) or moderate to severe asthma
- Significant cardiac disease (eg, heart failure, coronary artery disease, congenital heart disease, cardiomyopathies, and
- pulmonary hypertension)
- Severe obesity (body mass index ≥ 40 kg/m2)
- Diabetes (Type 1, Type 2 or gestational)
- Liver disease
- Human immunodeficiency virus (HIV) infection

*** Age and health risk for severe COVID-19 is used as stratification factor for randomization.

14.2 Study Results

The analysis of the primary efficacy endpoint included 28,207 participants 18 years of age and older (14,134 in the mRNA-1273 COVID-19 Vaccine group and 14,073 in the placebo group). At the time of the final primary efficacy analysis, participants had been followed for symptomatic COVID 19 disease for a median of 2 months after the second dose, corresponding to 3304.9 person years for the mRNA-1273 COVID-19 Vaccine and 3273.7 person years in the placebo group.

There were 11 confirmed COVID-19 cases identified in the mRNA-1273 COVID-19 Vaccine and 185 in placebo groups, respectively, for the primary efficacy analysis. Compared to placebo, efficacy of mRNA-1273 COVID-19 Vaccine in participants with first COVID-19 occurrence from 14 days after Dose 2 was 94.1% (two-sided 95% confidence interval of 89.3% to 96.8%). In participants 65 years of age and older, efficacy of mRNA-1273 COVID-19 Vaccine was 86.4% (two-sided 95% confidence interval of 61.4%% to 95.5%). At the time of primary efficacy analysis, there was a total of 30 severe COVID-19 cases starting 14 days after dose 2, per adjudication committee assessment. All 30 cases were in the placebo group.

15 MICROBIOLOGY

No microbiological information is required for this vaccine product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: Intramuscular administration of COVID-19 Vaccine Moderna (or other Moderna mRNA investigational vaccines) at doses ranging from 9 to 150 mcg/dose administered once every 2 weeks for up to 6 weeks resulted in transient injection site erythema and edema, body temperature increases, and a generalized systemic inflammatory response. Transient hepatocyte vacuolation and/or Kupffer cell hypertrophy, often observed without liver enzyme elevations, was observed and considered secondary to the systemic inflammatory response. In general, all changes resolved within 2 weeks.

Carcinogenicity: COVID-19 Vaccine Moderna has not been evaluated for carcinogenicity in animals, as carcinogenicity studies were not considered relevant to this vaccine.

Genotoxicity: SM-102, a proprietary lipid component of COVID-19 Vaccine Moderna, is not genotoxic in the bacterial mutagenicity and the human peripheral blood lymphocytes chromosome aberration assays. Two intravenous in vivo micronucleus assays were conducted with mRNA therapies using the

same lipid nanoparticle (LNP) formulation as COVID-19 Vaccine Moderna. Equivocal results observed at high systemic concentrations were likely driven by micronuclei formation secondary to elevated body temperature induced by a LNP-driven systemic inflammatory response. The genotoxic risk to humans is considered to be low due to minimal systemic exposure following intramuscular administration, limited duration of exposure, and the negative in vitro results.

Reproductive and Developmental Toxicology: In a pre- and post-natal developmental toxicity study, 0.2mL of a vaccine formulation containing the same quantity of mRNA (100 µg) and other ingredients included in a single human dose of COVID-19 Vaccine Moderna was administered to female rats by the intramuscular route on four occasions: 28 and 14 days prior to mating, and on gestation days 1 and 13. No vaccine-related adverse effects on female fertility, fetal development or postnatal development were reported in the study.