

## SUMMARY OF PRODUCT CHARACTERISTICS

▼ 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 adverse reactions. See section 4.8 for how to report adverse reactions.

### 1 NAME OF THE MEDICINAL PRODUCT

Spikevax dispersion for injection  
COVID-19 mRNA Vaccine (nucleoside modified)

### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

This is a multidose vial which contains 10 doses of 0.5 mL.

One dose (0.5 mL) contains 100 micrograms of messenger RNA (mRNA) (embedded in SM-102 lipid nanoparticles).

Single-stranded, 5'-capped messenger RNA (mRNA) produced using a cell-free in vitro transcription from the corresponding DNA templates, encoding the viral spike (S) protein of SARS-CoV-2.

For the full list of excipients, see section 6.1.

### 3 PHARMACEUTICAL FORM

Dispersion for injection  
White to off white dispersion (pH: 7.0 – 8.0).

### 4 CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

Spikevax is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 12 years of age and older.

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

#### 4.2 Posology and method of administration

##### Posology

Individuals 12 years of age and older

Spikevax is administered as a course of 2 doses (0.5 mL each). It is recommended to administer the second dose 28 days after the first dose (see sections 4.4 and 5.1).

There are no data available on the interchangeability of Spikevax with other COVID-19 vaccines to complete the vaccination course. Individuals who have received the first dose of Spikevax should receive the second dose of Spikevax to complete the vaccination course.

*Severely immunocompromised aged 12 years and older*

A third dose may be given at least 28 days after the second dose to individuals who are severely immunocompromised (see section 4.4).

*Paediatric population*

The safety and efficacy of Spikevax in children less than 12 years of age have not yet been established. No data are available.

*Elderly population*

No dosage adjustment is required in elderly individuals  $\geq 65$  years of age.

Method of administration

The vaccine should be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm.

The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.

For precautions to be taken before administering the vaccine, see section 4.4.

For instructions regarding thawing, handling and disposal of the vaccine, see section 6.6.

### **4.3 Contraindications**

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

### **4.4 Special warnings and precautions for use**

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Hypersensitivity and anaphylaxis

Anaphylaxis has been reported in individuals who have received Spikevax. Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic reaction following administration of the vaccine.

Close observation for at least 15 minutes is recommended following vaccination. The second dose of the vaccine should not be given to those who have experienced severe allergic reactions (e.g. anaphylaxis, generalised urticaria) to the first dose of Spikevax.

#### Myocarditis and pericarditis

There have been very rare reports of myocarditis and pericarditis occurring after vaccination with Spikevax, often in younger men and shortly after the second dose of the vaccine. These are typically mild cases and individuals tend to recover within a short time following standard treatment and rest.

Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinated individuals should also seek immediate medical attention should they experience new onset of chest pain, shortness of breath, palpitations or arrhythmias.

#### Anxiety-related reactions

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.

#### Concurrent illness

Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination.

#### Thrombocytopenia and coagulation disorders

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.

#### Immunocompromised individuals

The efficacy and safety of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of Spikevax may be lower in immunocompromised individuals.

The recommendation to consider a third dose (0.5 mL) in severely immunocompromised individuals (see section 4.2) is based on limited serological evidence with patients who are immunocompromised after solid organ transplantation.

### Duration of protection

The duration of protection afforded by the vaccine is unknown as it is still being determined by ongoing clinical trials.

### Limitations of vaccine effectiveness

Individuals may not be fully protected until 14 days after their second dose. As with all vaccines, vaccination with Spikevax may not protect all vaccine recipients.

### Excipients with known effect

#### *Sodium*

This vaccine contains less than 1 mmol sodium (23 mg) per 0.5 mL dose, that is to say, essentially 'sodium-free'.

## **4.5 Interaction with other medicinal products and other forms of interaction**

No interaction studies have been performed.

Concomitant administration of Spikevax with other vaccines has not been studied.

## **4.6 Fertility, pregnancy and lactation**

### Pregnancy

There is limited experience with use of Spikevax in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development (see section 5.3). Administration of Spikevax in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus.

### Breast-feeding

It is unknown whether Spikevax is excreted in human milk.

### Fertility

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

## **4.7 Effects on ability to drive and use machines**

Spikevax has no or negligible influence on the ability to drive and use machines.

However, some of the effects mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

## 4.8 Undesirable effects

### Summary of the safety profile

#### *Participants 18 years of age and older*

The safety of Spikevax was evaluated in an ongoing Phase 3 randomised, placebo-controlled, observer-blind clinical study conducted in the United States involving 30,351 participants 18 years of age and older who received at least one dose of Spikevax (n=15,185) or placebo (n=15,166) (NCT04470427). At the time of vaccination, the mean age of the population was 52 years (range 18-95); 22,831 (75.2%) of participants were 18 to 64 years of age and 7,520 (24.8%) of participants were 65 years of age and older.

The most frequently reported adverse reactions were pain at the injection site (92%), fatigue (70%), headache (64.7%), myalgia (61.5%), arthralgia (46.4%), chills (45.4%), nausea/vomiting (23%), axillary swelling/tenderness (19.8%), fever (15.5%), injection site swelling (14.7%) and redness (10%). Adverse reactions were usually mild or moderate in intensity and resolved within a few days after vaccination. A slightly lower frequency of reactogenicity events was associated with greater age.

Overall, there was a higher incidence of some adverse reactions in younger age groups: the incidence of axillary swelling/tenderness, fatigue, headache, myalgia, arthralgia, chills, nausea/vomiting and fever was higher in adults aged 18 to < 65 years than in those aged 65 years and above.

Local and systemic adverse reactions were more frequently reported after Dose 2 than after Dose 1.

If required, symptomatic treatment with analgesic and/or anti-pyretic medicinal products (e.g. paracetamol-containing products) may be used.

#### *Adolescents 12 through 17 years of age*

Safety data for Spikevax in adolescents were collected in an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical study conducted in the United States involving 3,726 participants 12 through 17 years of age who received at least one dose of Spikevax (n=2,486) or placebo (n=1,240) (NCT04649151). Demographic characteristics were similar among participants who received Spikevax and those who received placebo.

The most frequent adverse reactions in adolescents 12 to 17 years of age were injection site pain (97%), headache (78%), fatigue (75%), myalgia (54%), chills (49%), axillary swelling/tenderness (35%), arthralgia (35%), nausea/vomiting (29%), injection site swelling (28%), injection site erythema (26%), and fever (14%).

Tabulated list of adverse reactions from clinical studies and post-authorisation experience in individuals 12 years of age and older

The safety profile presented below is based on data generated in a placebo-controlled clinical study on 30,351 adults  $\geq 18$  years of age, another placebo-controlled clinical study with 3,726 participants 12 through 17 years of age, and post-marketing experience.

Adverse reactions reported are listed according to the following frequency convention:

Very common ( $\geq 1/10$ )

Common ( $\geq 1/100$  to  $< 1/10$ )

Uncommon ( $\geq 1/1,000$  to  $< 1/100$ )

Rare ( $\geq 1/10,000$  to  $< 1/1,000$ )

Very rare ( $< 1/10,000$ )

Not known (cannot be estimated from the available data)

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness (Table 1).

**Table 1 Adverse reactions from Spikevax clinical trials and post-authorisation experience in individuals 12 years of age and older**

MedDRA System Organ Class	Frequency	Adverse reactions
<b>Blood and lymphatic system disorders</b>	Very common	Lymphadenopathy*
<b>Immune system disorders</b>	Not known	Anaphylaxis
	Not known	Hypersensitivity
<b>Nervous system disorders</b>	Very common	Headache
	Uncommon	Dizziness
	Rare	Acute peripheral facial paralysis** Hypoesthesia
<b>Cardiac disorders</b>	Not known	Myocarditis Pericarditis
<b>Gastrointestinal disorders</b>	Very common	Nausea/vomiting
	Common	Diarrhoea
<b>Skin and subcutaneous tissue disorders</b>	Common	Rash
<b>Musculoskeletal and connective tissue disorders</b>	Very common	Myalgia Arthralgia
<b>General disorders and administration site conditions</b>	Very common	Injection site pain Fatigue Chills Pyrexia Injection site swelling

	Common	Injection site erythema Injection site urticaria Injection site rash Delayed injection site reaction***
	Uncommon	Injection site pruritus
	Rare	Facial swelling face****

\*Lymphadenopathy was captured as axillary lymphadenopathy on the same side as the injection site. Other lymph nodes (e.g., cervical, supraclavicular) were affected in some cases.

\*\*Throughout the safety follow-up period, acute peripheral facial paralysis (or palsy) was reported by three participants in the Spikevax group and one participant in the placebo group. Onset in the vaccine group participants was 22 days, 28 days, and 32 days after Dose 2.

\*\*\* Median time to onset was 9 days after the first injection, and 11 days after the second injection. Median duration was 4 days after the first injection, and 4 days after the second injection.

\*\*\*\*There were two serious adverse events of facial swelling in vaccine recipients with a history of injection of dermatological fillers. The onset of swelling was reported on Day 1 and Day 3, respectively, relative to day of vaccination.

The reactogenicity and safety profile in 343 subjects receiving Spikevax, that were seropositive for SARS-CoV-2 at baseline, was comparable to that in subjects seronegative for SARS-CoV-2 at baseline.

#### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. If you are concerned about an adverse event, it should be reported on a Yellow Card. Reporting forms and information can be found at <https://coronavirus-yellowcard.mhra.gov.uk/> or search for MHRA Yellow Card in the Google Play or Apple App Store and include the vaccine brand and batch/Lot number if available. Alternatively, adverse events of concern in association with Spikevax can be reported to Moderna on the toll-free number: 08000857562 or via [www.modernacovid19global.com](http://www.modernacovid19global.com). Please do not report the same adverse event(s) to both systems as all reports will be shared between Moderna and MHRA (in an anonymised form) and dual reporting will create unnecessary duplicates.

#### **4.9 Overdose**

No case of overdose has been reported.  
In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

### **5 PHARMACOLOGICAL PROPERTIES**

#### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Vaccine, other viral vaccines, ATC code: J07BX03

#### Mechanism of action





			<b>19 per 1,000 Person- Years</b>			<b>Person- Years</b>	
Overall (≥18)	14,134	11	3.328	14,073	185	56.510	94.1 (89.3, 96.8)**
18 to <65	10,551	7	2.875	10,521	156	64.625	95.6 (90.6, 97.9)
≥65	3,583	4	4.595	3,552	29	33.728	86.4 (61.4, 95.2)
≥65 to <75	2,953	4	5.586	2,864	22	31.744	82.4% (48.9, 93.9)
≥75	630	0	0	688	7	41.968	100% (NE, 100)

#COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the 2<sup>nd</sup> dose.

\*Vaccine efficacy and 95% confidence interval (CI) from the stratified Cox proportional hazard model

\*\* CI not adjusted for multiplicity. Multiplicity adjusted statistical analyses were carried out in an interim analysis based on less COVID-19 cases, not reported here.

Among all subjects in the PPS, no cases of severe COVID-19 were reported in the vaccine group compared with 30 of 185 (16%) cases reported in the placebo group.

Of the 30 participants with severe disease, 9 were hospitalised, 2 of which were admitted to an intensive care unit. The majority of the remaining severe cases fulfilled only the oxygen saturation (SpO<sub>2</sub>) criterion for severe disease (≤ 93% on room air).

The vaccine efficacy of Spikevax to prevent COVID-19, regardless of prior SARS-CoV-2 infection (determined by baseline serology and nasopharyngeal swab sample testing) from 14 days after Dose 2 was 93.6% (95% confidence interval 88.5, 96.4%).

Additionally, subgroup analyses of the primary efficacy endpoint showed similar efficacy point estimates across genders, ethnic groups, and participants with medical comorbidities associated with high risk of severe COVID-19.

The level of protection gained after dose 1 was assessed in a post-hoc analysis in the mITT Set. In the interval 14 days after dose 1 to dose 2, there were 35 cases of COVID-19 on placebo and only 2 in the vaccine group. This indicates that the vaccine may provide some level of protection from 14 days after the first dose and before receiving dose 2. For optimal protection, two doses should be administered one month apart.

#### Clinical efficacy in adolescents 12 through 17 years of age

The adolescent study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind clinical study (NCT04649151) to evaluate the safety, reactogenicity, and efficacy of Spikevax in adolescents 12 to 17 years of age. Participants with a known history of SARS-CoV-2 infection were excluded from

the study. A total of 3,732 participants were randomised 2:1 to receive 2 doses of Spikevax or saline placebo 1 month apart.

A secondary efficacy analysis was performed in 3,181 participants who received 2 doses of either Spikevax (n=2,139) or placebo (n=1,042) and had a negative baseline SARS-CoV-2 status in the Per Protocol Set. Between participants who received Spikevax and those who received placebo, there were no notable differences in demographics or pre-existing medical conditions.

COVID-19 was defined as symptomatic COVID-19 requiring positive RT-PCR result and at least 2 systemic symptoms or 1 respiratory symptom. Cases starting 14 days after the second dose: there were zero symptomatic COVID-19 cases in the Spikevax group and 4 symptomatic COVID-19 cases in the placebo group.

#### Immunogenicity in adolescents 12 through 17 years of age

A non-inferiority analysis evaluating SARS-CoV-2 50% neutralising titers and seroresponse rates 28 days after Dose 2 was conducted in the Per-Protocol immunogenicity subsets of adolescents aged 12 through 17 (n=340) in the adolescent study and in participants aged 18 through 25 (n=296) in the adult study. Subjects had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. The geometric mean ratio (GMR) of the neutralising antibody titers in adolescents 12 to 17 years of age compared to the 18- to 25-year-olds was 1.08 (95% CI: 0.94, 1.24). The difference in seroresponse rate was 0.2% (95% CI: -1.8, 2.4). Non-inferiority criteria (lower bound of the 95% CI for GMR > 0.67 and lower bound of the 95% CI of the seroresponse rate difference > -10%) were met.

#### Elderly population

Spikevax was assessed in individuals 12 years of age and older, including 3,768 subjects 65 years of age and older. The efficacy of Spikevax was consistent between elderly ( $\geq 65$  years) and younger adult subjects (18-64 years).

#### Paediatric population

The licensing authority has deferred the obligation to submit the results of studies with Spikevax in one or more subsets of the paediatric population in prevention of COVID-19 (see section 4.2 for information on paediatric use).

#### Conditional approval

This medicinal product has been authorised under a so-called 'conditional approval' scheme. This means that further evidence on this medicinal product is awaited. New information on this medicinal product will be reviewed at least every year and this SmPC will be updated as necessary.

## **5.2 Pharmacokinetic properties**

Not applicable.

## **5.3 Preclinical safety data**

Non-clinical data reveal no special hazard for humans based on conventional studies of repeat dose toxicity and reproductive and developmental toxicity. The full relevance of animal studies to human risk with vaccines for COVID-19 remains to be established.

#### General toxicity

General toxicity studies were conducted in rats (intramuscularly receiving up to 4 doses exceeding the human dose once every 2 weeks). Transient and reversible injection site oedema and erythema and transient and reversible changes in laboratory tests (including increases in eosinophils, activated partial thromboplastin time, and fibrinogen) were observed. Results suggests the toxicity potential to humans is low.

#### Genotoxicity/carcinogenicity

In vitro and in vivo genotoxicity studies were conducted with the novel lipid component SM-102 of the vaccine. Results suggests the genotoxicity potential to humans is very low. Carcinogenicity studies were not performed.

#### Reproductive toxicity

In a developmental toxicity study, 0.2 mL of a vaccine formulation containing the same quantity of mRNA (100 micrograms) and other ingredients included in a single human dose of Spikevax 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. SARS-CoV-2 antibody responses were present in maternal animals from prior to mating to the end of the study on lactation day 21 as well as in foetuses and offspring. There were no vaccine-related adverse effects on female fertility, pregnancy, embryo foetal or offspring development or postnatal development. No data are available of mRNA-1273 vaccine placental transfer or excretion in milk.

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

This vaccine contains polyethylene glycol/macrogol (PEG) as part of PEG2000-DMG.

Lipid SM-102 (heptadecan-9-yl 8-((2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino)octanoate)

Cholesterol

1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC)

1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG)

Trometamol

Trometamol hydrochloride

Acetic acid

Sodium acetate trihydrate

Sucrose

Water for injections

## 6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products or diluted.

## 6.3 Shelf life

### Unopened vial:

7 months at -25°C to -15°C.

The unopened vaccine may be stored refrigerated at 2°C to 8°C, protected from light, for maximum 30 days. Within this period, up to 12 hours may be used for transportation.

Once thawed the vaccine should not be re-frozen.

The unopened vaccine may be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions.

### Punctured vial:

Chemical and physical in-use stability has been demonstrated for 6 hours at 2°C to 25°C after initial puncture (within the allowed use period of 30 days at 2°C to 8°C and 24 hours at 8°C to 25°C). From a microbiological point of view, the product should be used immediately. If the vaccine is not used immediately, in-use storage times and conditions are the responsibility of the user.

## 6.4 Special precautions for storage

Store frozen between -25°C to -15°C.

Store in the original carton to protect from light.

Do not store on dry ice or below -50°C.

For storage conditions after thawing and first opening, see section 6.3.

### Transportation of thawed vials in liquid state at 2°C to 8°C

If transport at -50°C to -15°C is not feasible, available data support transportation of one or more thawed vials in liquid state for up to 12 hours at 2°C to 8°C (within the 30 days shelf life at 2°C to 8°C). Once thawed and transported in liquid state at 2°C to 8°C, vials should not be refrozen and should be stored at 2°C to 8°C until use.

## 6.5 Nature and contents of container

5 mL dispersion in a vial (type 1 or type 1 equivalent glass) with a stopper (chlorobutyl rubber) and a flip-off plastic cap with seal (aluminium seal).

Each vial contains 10 doses of 0.5 mL.

Pack size: 10 multidose vials

## 6.6 Special precautions for disposal

The vaccine should be prepared and administered by a trained healthcare professional using aseptic techniques to ensure sterility of the dispersion.

The vaccine comes ready to use once thawed.

Do not shake or dilute. Swirl the vial gently after thawing and before each withdrawal.

Spikevax vials are multidose.

Ten (10) doses (of 0.5mL each) can be withdrawn from each vial. Pierce the stopper preferably at a different site each time.

An additional overfill is included in each vial to ensure that 10 doses of 0.5 mL can be delivered.


Thawed vials and filled syringes can be handled in room light conditions.

### Frozen Storage

Can be stored frozen until expiry date

**-25° to -15°C**

Do not store on dry ice or below -50°C  
Store in the original carton to protect from light.



### Thaw Each Vial Before Use

Vial images for illustrative purposes only

**2 hours and 30 minutes in refrigerator**

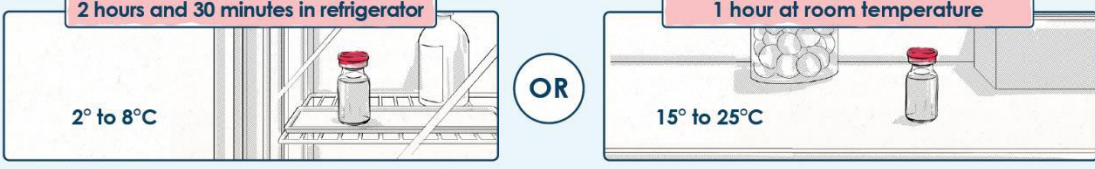
**2° to 8°C**

**OR**

**1 hour at room temperature**

**15° to 25°C**

Let vial sit at room temperature for 15 minutes before administering



## Instructions Once Thawed

Unpunctured Vial		After first dose has been withdrawn	
<b>30 days</b>	Maximum times Refrigerator 2° to 8°C	<b>6 hours</b>	Maximum time Refrigerator or room temperature
<b>24 hours</b>	Cool storage up to room temperature 8° to 25°C	Vial should be held between 2° to 25°C. Record the date and time of discard on the vial label. Discard punctured vial after 6 hours.	



Withdraw each 0.5 mL dose of vaccine from the vial using a new sterile needle and syringe for each injection to prevent transmission of infectious agents from one person to another. **The dose in the syringe should be used immediately.**

**Once the vial has been punctured to withdraw the initial dose, the vaccine should be used immediately and be discarded after 6 hours.**

Any unused vaccine or waste material should be disposed of in accordance with local requirements.

**NEVER refreeze thawed vaccine**

## Administration

Swirl vial gently after thawing and before each withdrawal.  
The vaccine comes ready to use once thawed. **Do not shake or dilute.**

**Prior to injection, inspect each dose to:**

Confirm liquid is **white to off-white** in colour in both vial and syringe

Verify syringe volume of **0.5 mL**

The COVID-19 Vaccine Moderna may contain white or translucent product-related particulates.

If dosage is incorrect, or discolouration and other particulate matter is present, do not administer the vaccine.



### 7 MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.  
Calle Monte Esquinza 30  
28010 Madrid  
Spain

### 8 MARKETING AUTHORISATION NUMBER(S)

PLGB 53720/0002

### 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

31/03/2021

**10 DATE OF REVISION OF THE TEXT**

1/12/2021