ANNEX I

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 0.2 mg/mL dispersion for injection  
Spikevax 0.1 mg/mL dispersion for injection  
Spikevax 50 micrograms dispersion for injection in pre-filled syringe  
COVID-19 mRNA Vaccine (nucleoside modified)

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

Table 1. Qualitative and quantitative composition by strength and type of container

<table>
<thead>
<tr>
<th>Strength</th>
<th>Container</th>
<th>Dose(s)</th>
<th>Composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spikevax 0.2 mg/mL dispersion for injection</td>
<td>Multidose vial (red flip-off cap)</td>
<td>Maximum 10 doses of 0.5 mL each</td>
<td>One dose (0.5 mL) contains 100 micrograms of elasomeran, a COVID-19 mRNA Vaccine (embedded in lipid nanoparticles).</td>
</tr>
<tr>
<td> </td>
<td> </td>
<td>Maximum 20 doses of 0.25 mL each</td>
<td>One dose (0.25 mL) contains 50 micrograms of elasomeran, a COVID-19 mRNA Vaccine (embedded in lipid nanoparticles).</td>
</tr>
<tr>
<td>Spikevax 0.1 mg/mL dispersion for injection and Spikevax 50 micrograms dispersion for injection in pre-filled syringe</td>
<td>Multidose vial (blue flip-off cap)</td>
<td>5 doses of 0.5 mL each</td>
<td>One dose (0.5 mL) contains 50 micrograms of elasomeran, a COVID-19 mRNA Vaccine (embedded in lipid nanoparticles).</td>
</tr>
<tr>
<td> </td>
<td>Pre-filled syringe</td>
<td>1 dose of 0.5 mL For single-use only.</td>
<td>One dose (0.5 mL) contains 50 micrograms of elasomeran, a COVID-19 mRNA Vaccine (embedded in lipid nanoparticles).</td>
</tr>
</tbody>
</table>

Elasomeran is a 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 6 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

Refer to Table 2 for dosing across Spikevax strengths and vaccination type.

**Table 2. Spikevax posology for primary series, a third dose in severely immunocompromised and booster doses**

<table>
<thead>
<tr>
<th>Strength</th>
<th>Vaccination type</th>
<th>Age(s)</th>
<th>Dose</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spikevax 0.2 mg/mL dispersion for injection</td>
<td>Primary series</td>
<td>Individuals 12 years of age and older</td>
<td>2 (two) doses (0.5 mL each, containing 100 micrograms mRNA)</td>
<td>It is recommended to administer the second dose 28 days after the first dose (see sections 4.4 and 5.1).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Children 6 through 11 years of age</td>
<td>2 (two) doses (0.25 mL each, containing 50 micrograms mRNA, which is half of the primary dose for individuals 12 years and older)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Third dose in severely immunocompromised</td>
<td>Individuals 12 years of age and older</td>
<td>1 (one) dose of 0.5 mL, containing 100 micrograms mRNA</td>
<td>A third dose may be given at least 28 days after the second dose (see section 4.4).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Children 6 through 11 years of age</td>
<td>1 (one) dose of 0.25 mL, containing 50 micrograms mRNA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Booster dose</td>
<td>Individuals 12 years of age and older</td>
<td>1 (one) dose of 0.25 mL, containing 50 micrograms mRNA</td>
<td>Spikevax may be used to boost individuals 12 years of age and older who have received a primary series with Spikevax or a primary series comprised of another mRNA vaccine or adenoviral vector vaccine at least 3 months after</td>
</tr>
<tr>
<td>Strength</td>
<td>Vaccination type</td>
<td>Age(s)</td>
<td>Dose</td>
<td>Recommendations</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>-----------------------------------------</td>
<td>-----------------------------------------</td>
<td>----------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Spikevax 0.1 mg/mL dispersion</td>
<td>Primary series*</td>
<td>Children 6 years through 11 years of age</td>
<td>2 (two) doses (0.5 mL each, containing 50 micrograms mRNA each)</td>
<td>It is recommended to administer the second dose 28 days after the first dose (see sections 4.4 and 5.1).</td>
</tr>
<tr>
<td>for injection and Spikevax 50</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>micrograms dispersion for</td>
<td>Third dose in severely immunocompromised†</td>
<td>Children 6 years through 11 years of age</td>
<td>1 (one) dose of 0.5 mL, containing 50 micrograms mRNA</td>
<td>A third dose may be given at least 28 days after the second dose (see sections 4.4 and 5.1).</td>
</tr>
<tr>
<td>in pre-filled syringe</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Booster dose</td>
<td>Individuals 12 years of age and older</td>
<td></td>
<td>1 (one) dose of 0.5 mL, containing 50 micrograms mRNA</td>
<td>Spikevax may be used to boost individuals 12 years of age and older who have received a primary series with Spikevax or a primary series comprised of another mRNA vaccine or adenoviral vector vaccine at least 3 months after completion of the primary series (see section 5.1).</td>
</tr>
</tbody>
</table>

*For primary series for individuals 12 years of age and older, the 0.2 mg/mL strength vial should be used.
†For the third dose in severely immunocompromised patients 12 years of age and older, the 0.2 mg/mL strength vial should be used.

**Paediatric population**
The safety and efficacy of Spikevax in children less than 6 years of age have not yet been established. No data are available.

**Elderly**
No dose adjustment is required in elderly individuals ≥65 years of age.

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

Do not administer this vaccine intravascularly, subcutaneously or intradermally.

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. Subsequent doses of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of Spikevax.

**Myocarditis and pericarditis**

There is an increased risk for myocarditis and pericarditis following vaccination with Spikevax.

These conditions can develop within just a few days after vaccination, and have primarily occurred within 14 days. They have been observed more often after the second dose compared to the first dose, and more often in younger males (see section 4.8). The risk profile appears to be similar for the second and the third dose.

Available data suggest that the course of myocarditis and pericarditis following vaccination is not different from myocarditis or pericarditis in general.

Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccinees should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis such as (acute and persisting) chest pain, shortness of breath, or palpitations following vaccination.

Healthcare professionals should consult guidance and/or specialists to diagnose and treat this condition.

**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.

**Capillary leak syndrome flare-ups**

A few cases of capillary leak syndrome (CLS) flare-ups have been reported in the first days after vaccination with Spikevax. Healthcare professionals should be aware of signs and symptoms of CLS to promptly recognise and treat the condition. In individuals with a medical history of CLS, planning of vaccination should be made in collaboration with appropriate medical experts.

**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 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 studies.

**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), 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**

A large amount of observational data from pregnant women vaccinated with Spikevax during the second and third trimester has not shown an increase in adverse pregnancy outcomes. While data on pregnancy outcomes following vaccination during the first trimester are presently limited, no increased risk for miscarriage has been seen. 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). Spikevax can be used during pregnancy.

**Breast-feeding**
No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breastfeeding woman to Spikevax is negligible. Observational data from women who were breastfeeding after vaccination have not shown a risk for adverse effects in breastfed newborns/infants. Spikevax can be used during breastfeeding.

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.

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%).

Children 6 through 11 years of age

Safety data for Spikevax in children were collected in an ongoing Phase 2/3 two-part randomised, observer-blind clinical study conducted in the United States and Canada (NCT04796896). Part 1 is an open-label phase of the study for safety, dose selection, and immunogenicity and included 380 participants 6 through 11 years of age who received at least 1 dose (0.25 mL) of Spikevax. Part 2 is the placebo-controlled phase for safety and included 4 016 participants 6 through 11 years of age.
who received at least one dose (0.25 mL) of Spikevax (n=3 012) or placebo (n=1 004). No participants in Part 1 participated in Part 2. Demographic characteristics were similar among participants who received Spikevax and those who received placebo.

The most frequent adverse reactions in participants 6 through 11 years of age following administration of the primary series were injection site pain (98.4%), fatigue (73.1%), headache (62.1%), myalgia (35.3%), chills (34.6%), nausea/vomiting (29.3%), axillary swelling/tenderness (27.0%), fever (25.7%), injection site erythema (24.0%), injection site swelling (22.3%), and arthralgia (21.3%).

Tabulated list of adverse reactions from clinical studies and post authorisation experience in children and individuals 6 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 ≥ 18 years of age, another placebo-controlled clinical study with 3 726 adolescents 12 through 17 years of age, another clinical study with 4 002 children 6 years through 11 years of age, and post-marketing experience.

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

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1 000 to <1/100)
Rare (≥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 3).

Table 3. Adverse reactions from Spikevax clinical studies and post authorisation experience in children and individuals 6 years of age and older

<table>
<thead>
<tr>
<th>MedDRA system organ class</th>
<th>Frequency</th>
<th>Adverse reaction(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Very common</td>
<td>Lymphadenopathy*</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>Not known</td>
<td>Anaphylaxis Hypersensitivity</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Very common</td>
<td>Headache</td>
</tr>
<tr>
<td></td>
<td>Uncommon</td>
<td>Dizziness</td>
</tr>
<tr>
<td></td>
<td>Rare</td>
<td>Acute peripheral facial paralysis** Hypoaesthesia Paraesthesia</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td>Very rare</td>
<td>Myocarditis Pericarditis</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Very common</td>
<td>Nausea/vomiting</td>
</tr>
<tr>
<td></td>
<td>Common</td>
<td>Diarrhoea</td>
</tr>
<tr>
<td></td>
<td>Uncommon</td>
<td>Abdominal pain***</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Common</td>
<td>Rash</td>
</tr>
<tr>
<td></td>
<td>Not known</td>
<td>Erythema multiforme</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>Very common</td>
<td>Myalgia Arthralgia</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Very common</td>
<td>Injection site pain Fatigue Chills Pyrexia Injection site swelling</td>
</tr>
<tr>
<td>MedDRA system organ class</td>
<td>Frequency</td>
<td>Adverse reaction(s)</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------</td>
<td>---------------------</td>
</tr>
<tr>
<td></td>
<td>Common</td>
<td>Injection site erythema</td>
</tr>
<tr>
<td>Common</td>
<td>Injection site urticaria</td>
<td></td>
</tr>
<tr>
<td>Common</td>
<td>Injection site rash</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Injection site rash</td>
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<tr>
<td></td>
<td>Injection site rash</td>
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<tr>
<td></td>
<td>Injection site rash</td>
<td></td>
</tr>
<tr>
<td>Uncommon</td>
<td>Delayed injection site reaction****</td>
<td></td>
</tr>
<tr>
<td>Rare</td>
<td>Injection site pruritus</td>
<td></td>
</tr>
<tr>
<td>Not known</td>
<td>Not known</td>
<td></td>
</tr>
</tbody>
</table>

* 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.

*** Abdominal pain was observed in the paediatric population (6 to 11 years of age): 0.2% in the Spikevax group and 0% in the placebo group.

****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.

Participants 18 years of age and older (booster dose)
The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax are evaluated in an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL, 100 micrograms 1 month apart) of the Spikevax vaccine primary series. In an open-label phase of this study, 167 of those participants received a single booster dose (0.25 mL, 50 micrograms) at least 6 months after receiving the second dose of the primary series. The solicited adverse reaction profile for the booster dose (0.25 mL, 50 micrograms) was similar to that after the second dose in the primary series.

Description of selected adverse reactions

**Myocarditis**
The increased risk of myocarditis after vaccination with Spikevax is highest in younger males (see section 4.4).

Two large European pharmacoepidemiological studies have estimated the excess risk in younger males following the second dose of Spikevax. One study showed that in a period of 7 days after the second dose, there were about 1.316 (95% CI 1.299 – 1.333) extra cases of myocarditis in 12 to 29 year-old males per 10 000 compared to unexposed persons. In another study, in a period of 28 days after the second dose, there were 1.88 (95% CI 0.956 – 2.804) extra cases of myocarditis in 16 to 24 year-old males per 10 000 compared to unexposed persons.

**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. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V and include batch/Lot number if available.

**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

Spikevax (elasomeran) contains mRNA encapsulated in lipid nanoparticles. The mRNA encodes for the full-length SARS-CoV-2 spike protein modified with 2 proline substitutions within the heptad repeat 1 domain (S-2P) to stabilise the spike protein into a prefusion conformation. After intramuscular injection, cells at the injection site and the draining lymph nodes take up the lipid nanoparticle, effectively delivering the mRNA sequence into cells for translation into viral protein. The delivered mRNA does not enter the cellular nucleus or interact with the genome, is non-replicating, and is expressed transiently mainly by dendritic cells and subcapsular sinus macrophages. The expressed, membrane-bound spike protein of SARS-CoV-2 is then recognised by immune cells as a foreign antigen. This elicits both T-cell and B-cell responses to generate neutralising antibodies, which may contribute to protection against COVID-19.

Clinical efficacy in adults

The adult study was a randomised, placebo-controlled, observer-blind Phase 3 clinical study (NCT04470427) that excluded individuals who were immunocompromised or had received immunosuppressants within 6 months, as well as participants who were pregnant, or with a known history of SARS-CoV-2 infection. Participants with stable HIV disease were not excluded. Influenza vaccines could be administered 14 days before or 14 days after any dose of Spikevax. Participants were also required to observe a minimum interval of 3 months after receipt of blood/plasma products or immunoglobulins prior to the study in order to receive either placebo or Spikevax.

A total of 30,351 subjects were followed for a median of 92 days (range: 1-122) for the development of COVID-19 disease.

The primary efficacy analysis population (referred to as the Per Protocol Set or PPS), included 28,207 subjects who received either Spikevax (n=14,134) or placebo (n=14,073) and had a negative baseline SARS-CoV-2 status. The PPS study population included 47.4% female, 52.6% male, 79.5% White, 9.7% African American, 4.6% Asian, and 6.2% other. 19.7% of participants identified as Hispanic or Latino. The median age of subjects was 53 years (range 18-94). A dosing window of -7 to +14 days for administration of the second dose (scheduled at day 29) was allowed for inclusion in the PPS. 98% of vaccine recipients received the second dose 25 days to 35 days after dose 1 (corresponding to -3 to +7 days around the interval of 28 days).

COVID-19 cases were confirmed by Reverse Transcriptase Polymerase Chain Reaction (RT PCR) and by a Clinical Adjudication Committee. Vaccine efficacy overall and by key age groups are presented in Table 4.
Table 4. Vaccine efficacy analysis: confirmed COVID-19# regardless of severity starting 14 days after the 2nd dose – per-protocol set

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Spikevax</th>
<th>Placebo</th>
<th>% Vaccine efficacy (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Subjects N</td>
<td>COVID-19 cases</td>
<td>Incidence rate of COVID-19 per 1 000 person-years</td>
</tr>
<tr>
<td>Overall (≥18)</td>
<td>14 134</td>
<td>11</td>
<td>3.328</td>
</tr>
<tr>
<td>18 to &lt;65</td>
<td>10 551</td>
<td>7</td>
<td>2.875</td>
</tr>
<tr>
<td>≥65</td>
<td>3 583</td>
<td>4</td>
<td>4.595</td>
</tr>
<tr>
<td>≥65 to &lt;75</td>
<td>2 953</td>
<td>4</td>
<td>5.586</td>
</tr>
<tr>
<td>≥75</td>
<td>630</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

#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 2nd 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 (SpO2) 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 88.6, 96.5%).

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.

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 to 17 years of age

A non-inferiority analysis evaluating SARS-CoV-2 50% neutralising titres 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 titres 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.

Clinical efficacy in children 6 through 11 years of age

The paediatric study is an ongoing Phase 2/3 randomised, placebo-controlled, observer-blind, clinical study to evaluate the safety, reactogenicity, and effectiveness of Spikevax in children aged 6 through 11 years in the United States and Canada (NCT04796896). Participants with a known history of SARS-CoV-2 infection were excluded from the study. A total of 4 011 participants were randomised 3:1 to receive 2 doses of Spikevax or saline placebo 1 month apart.

A secondary efficacy analysis evaluating confirmed COVID-19 cases accrued up to the data cutoff date of 10 November 2021 was performed in 3 497 participants who received two doses (0.25 mL at 0 and 1 month) of either Spikevax (n=2 644) or placebo (n=853) 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.

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 three COVID-19 cases (0.1%) in the Spikevax group and four COVID-19 cases (0.5%) in the placebo group.

Immunogenicity in children 6 through 11 years of age

An analysis evaluating SARS-CoV-2 50% neutralising titres and seroresponse rates 28 days after Dose 2 was conducted in a subset of children aged 6 through 11 years (n=319) in the paediatric study and in participants aged 18 through 25 years (n=295) in the adult study. Subjects had no immunologic or virologic evidence of prior SARS-CoV-2 infection at baseline. The GMR of the neutralising antibody titres in children 6 through 11 years of age compared to the 18- to 25-year-olds was 1.239 (95% CI: 1.072, 1.432). The difference in seroresponse rate was 0.1% (95% CI: -1.9, 2.1). 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.

Immunogenicity in participants 18 years of age and older – after booster dose (0.25 mL, 50 micrograms)

The safety, reactogenicity, and immunogenicity of a booster dose of Spikevax are evaluated in an ongoing Phase 2, randomised, observer-blind, placebo-controlled, dose-confirmation study in participants 18 years of age and older (NCT04405076). In this study, 198 participants received two doses (0.5 mL, 100 micrograms 1 month apart) of the Spikevax vaccine as primary series. In an open-label phase, 149 of those participants (Per-Protocol Set) received a single booster dose (0.25 mL, 50 micrograms) at least 6 months after receiving the second dose in the primary series. A single booster dose (0.25 mL, 50 micrograms) was shown to result in a geometric mean fold rise (GMFR) of 12.99 (95% CI: 11.04, 15.29) in neutralising antibodies from pre-booster compared to 28 days after
the booster dose. The GMFR in neutralising antibodies was 1.53 (95% CI: 1.32, 1.77) when compared 28 days post dose 2 (primary series) to 28 days after the booster dose.

**Immunogenicity of a booster dose following primary vaccination with another authorised COVID-19 vaccine in adults 18 years of age and older**

Safety and immunogenicity of a heterologous booster with Spikevax were studied in an investigator-initiated study with 154 participants. The minimum time interval between primary series using a vector-based or RNA-based COVID-19 vaccine and booster injection with Spikevax was 12 weeks (range: 12 weeks to 20.9 weeks). The dose used for boosting in this study was 100 micrograms. Neutralising antibody titres as measured by a pseudovirus neutralisation assay were assessed on Day 1 prior to administration and at Day 15 and Day 29 after the booster dose. A booster response was demonstrated regardless of primary vaccination.

Only short-term immunogenicity data are available; long-term protection and immunological memory are currently unknown.

**Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) in the UK**

COV-BOOST is a multicentre, randomised Phase 2 investigator-initiated study of third dose booster vaccination against COVID-19 with a subgroup to investigate detailed immunology. Participants were adults aged 30 years or older, in good physical health (mild to moderate well-controlled co-morbidities were permitted), who had received two doses of either Pfizer–BioNTech or Oxford–AstraZeneca (first dose in December 2020, January 2021 or February 2021), and were at least 84 days post second dose by the time of enrolment. Spikevax boosted antibody and neutralising responses and was well tolerated regardless of the prime series. The dose used for boosting in this study was 100 micrograms. Neutralising antibody titres as measured by a pseudovirus neutralisation assay were assessed on Day 28 after the booster dose.

**Pre-boost and post-boost neutralising antibody against the B.1.617.2 (Delta) variant in adults**

Results of the pseudovirus neutralisation assay (PsVNA) against the B.1.617.2 (Delta) variant determined pre-booster and on Day 29 post-booster showed that administration of a booster dose of Spikevax (0.25 mL, 50 micrograms) in adults induced a 17-fold rise in neutralising antibodies against the Delta variant compared with pre-booster levels (GMFR = 17.28; 95% CI: 14.38, 20.77; n=295).

**Neutralising antibody against the B.1.617.2 (Delta) variant in children 6 through 11 years of age**

Serum samples of the per-protocol immunogenicity subset (n=134) of the ongoing paediatric study obtained at baseline and on Day 57 were tested in a PsVNA based on the B.1.617.2 (Delta) variant. In children 6 through 11 years of age, the GMFR from baseline to D57 was 81.77 (95% CI: 70.38, 95.00) for the Delta variant (measured by PsVNA). Furthermore, 99.3% of children met the definition of seroresponse.

**Elderly**

Spikevax was assessed in individuals 6 years of age and older, including 3 768 subjects 65 years of age and older. The efficacy of Spikevax was consistent between elderly (≥65 years) and younger adult subjects (18-64 years).

**Paediatric population**

The European Medicines Agency has deferred the obligation to submit the results of studies with the 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. The European Medicines Agency will review new information on this medicinal product 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.

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 suggest 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 suggest 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 Spikevax vaccine placental transfer or excretion in milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

SM-102 (heptadecan-9-yl 8-\((2\text{-hydroxyethyl})[6\text{-oxo-6-(undecyloxy)hexyl}amino]\text{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 multidose vial (Spikevax 0.2 mg/mL dispersion for injection and Spikevax 0.1 mg/mL dispersion for injection)

9 months at -50ºC to -15ºC.

After removal from the freezer, the unopened vaccine vial may be stored refrigerated at 2ºC to 8ºC, protected from light, for a maximum of 30 days. Within this period, up to 12 hours may be used for transportation at 2ºC to 8ºC (see section 6.4).

Chemical and physical stability has also been demonstrated for unopened vaccine vials when stored for 12 months at -50ºC to -15ºC provided that once thawed and stored at 2ºC to 8ºC, protected from light, the unopened vial will be used up within a maximum of 14 days (instead of 30 days, when stored at -50ºC to -15ºC for 9 months).

Once thawed, the vaccine should not be re-frozen.

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

Punctured multidose vial (Spikevax 0.2 mg/mL dispersion for injection and Spikevax 0.1 mg/mL dispersion for injection)

Chemical and physical in-use stability has been demonstrated for 19 hours at 2ºC to 25ºC after initial puncture (within the allowed use period of 30 days at 2ºC to 8ºC and including 24 hours at 8ºC to 25ºC). 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.

Spikevax 50 micrograms dispersion for injection in pre-filled syringe

9 months at -50ºC to -15ºC.

After removal from the freezer, pre-filled syringes may be stored refrigerated at 2ºC to 8ºC, protected from light, for maximum 30 days. Within this period, pre-filled syringes may be transported up to 12 hours at 2ºC to 8ºC (see section 6.4).

Chemical and physical stability has also been demonstrated for unopened pre-filled syringes when stored for 12 months at -50ºC to -15ºC provided that once thawed and stored at 2ºC to 8ºC, protected from light, the pre-filled syringe will be used up within a maximum of 14 days (instead of 30 days, when stored at -50ºC to -15ºC for 9 months).

Once thawed, the vaccine should not be re-frozen.

Pre-filled syringes may be stored at 8ºC to 25ºC up to 24 hours after removal from refrigerated conditions.

6.4 Special precautions for storage

Multidose vials (Spikevax 0.2 mg/mL dispersion for injection and Spikevax 0.1 mg/mL dispersion for injection)

Store frozen between -50ºC to -15ºC.
Keep the vial in the outer carton to protect from light.
For storage conditions after thawing and first opening, see section 6.3.

Transportation of thawed multidose 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.

Spikevax 50 micrograms dispersion for injection in pre-filled syringe

Store frozen between -50°C to -15°C.
Keep the pre-filled syringe in the outer carton to protect from light.
For storage conditions after thawing and first opening, see section 6.3.

Transportation of thawed pre-filled syringes 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 pre-filled syringes 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, pre-filled syringes should not be refrozen and should be stored at 2°C to 8°C until use.

6.5 Nature and contents of container

Multidose vials

Spikevax 0.2 mg/mL dispersion for injection
5 mL dispersion in a (type 1 glass or type 1 equivalent glass or cyclic olefin polymer with inner barrier coating) multidose vial with a stopper (chlorobutyl rubber) and a red flip-off plastic cap with seal (aluminium seal).

Each vial contains 5 mL.

Pack size: 10 multidose vials

Spikevax 0.1 mg/mL dispersion for injection
2.5 mL dispersion in a (type 1 glass or type 1 equivalent glass or cyclic olefin polymer with inner barrier coating) multidose vial with a stopper (chlorobutyl rubber) and a blue flip-off plastic cap with seal (aluminium seal).

Each vial contains 2.5 mL.

Pack size: 10 multidose vials

Spikevax 50 micrograms dispersion for injection in pre-filled syringe

0.5 mL dispersion in a pre-filled syringe (polymeric) with plunger stopper (coated bromobutyl rubber) and a tip cap (bromobutyl rubber, without needle).

The pre-filled syringe is packaged in 5 clear blisters containing 2 pre-filled syringes in each blister.

Each pre-filled syringe contains 0.5 mL.

Pack size: 10 pre-filled syringes

6.6 Special precautions for disposal and other handling

The vaccine should be prepared and administered by a trained healthcare professional using aseptic techniques to ensure sterility of the dispersion.
Thawed vials and pre-filled syringes can be handled in room light conditions.

**Multidose vial**

The vaccine comes ready to use once thawed.

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

**Spikevax 0.2 mg/mL dispersion for injection**

A maximum of ten (10) doses (of 0.5 mL each) or a maximum of twenty (20) doses (of 0.25 mL each) can be withdrawn from each vial (red flip-off cap).

Pierce the stopper preferably at a different site each time. Do not puncture the vial more than 20 times.

An additional overfill is included in each vial to ensure that a maximum of 10 doses of 0.5 mL or a maximum of 20 doses of 0.25 mL can be delivered.

**Thaw each vial before use**

- 2 hours and 30 minutes in refrigerator
  - 2°C to 8°C
  - (within the 30 days shelf life of 2°C to 8°C)

- 1 hour at room temperature
  - 15°C to 25°C

Let vial sit at room temperature for 15 minutes before administering.

**Instructions Once Thawed**

*When stored for 12 months at 2°C to 8°C provided that once thawed and stored at 2°C to 8°C protected from light, the vial or pre-filled syringe should be used within a maximum of 34 days (instead of 30 days when stored at 2°C to 8°C for 9 months).*

Withdraw each 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.

Any unused vaccine or waste material should be disposed of in accordance with local requirements.
**Spikevax 0.1 mg/mL dispersion for injection**

Five (5) doses (of 0.5 mL each) can be withdrawn from each vial (blue flip-off cap).

Pierce the stopper preferably at a different site each time.

An additional overfill is included in each vial to ensure that 5 doses of 0.5 mL can be delivered.

**Spikevax 0.2 mg/mL dispersion for injection and Spikevax 0.1 mg/mL dispersion for injection**

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**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.

The vaccine 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.
Spikevax 50 micrograms dispersion for injection in pre-filled syringe

Do not shake or dilute the contents of the pre-filled syringe.

Each pre-filled syringe is for single use only. The vaccine comes ready to use once thawed.

One (1) dose of 0.5 mL can be administered from each pre-filled syringe.

Spikevax is supplied in a single-dose, pre-filled syringe (without needle) containing 0.5 mL (50 micrograms) mRNA and must be thawed prior to administration.

Thaw each pre-filled syringe before use following the instructions below. Syringes may be thawed in the blister packs (each blister containing 2 pre-filled syringes) or in the carton itself, either in the refrigerator or at room temperature (Table 5).

**Table 5. Thawing instructions for pre-filled syringes and cartons before use**

<table>
<thead>
<tr>
<th>Configuration</th>
<th>Thaw instructions and duration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Thaw Temperature (in a refrigerator) (°C)</td>
</tr>
<tr>
<td>Pre-filled syringe in blister pack</td>
<td>2 – 8</td>
</tr>
<tr>
<td>Carton</td>
<td>2 – 8</td>
</tr>
</tbody>
</table>

*Handling instructions for the pre-filled syringes*

- Let each pre-filled syringe stand at room temperature (15°C to 25°C) for 15 minutes before administering.
- Do not shake.
- Pre-filled syringe should be inspected visually for particulate matter and discoloration prior to administration.
- Spikevax is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discolored or contains other particulate matter.
- Needles are not included in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner needles).
- Remove tip cap from syringe by twisting in a counter-clockwise direction.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Uncap the needle when ready for administration.
- Administer the entire dose intramuscularly.
- Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. **MARKETING AUTHORISATION HOLDER**

MODERNA BIOTECH SPAIN, S.L.
Calle del Príncipe de Vergara 132 Plt 12
8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/001
EU/1/20/1507/002
EU/1/20/1507/003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 06 January 2021
Date of latest renewal: 04 October 2021

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.
ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORIZATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORIZATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORIZATION
A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers of the biological active substance

LONZA AG
Lonzastrasse
3930 Visp
Switzerland

ModernaTX, Inc.
One Moderna Way
Norwood, MA 02062
USA

Lonza Biologies, Inc.
101 International Drive Portsmouth, NH 03801
USA

Name and address of the manufacturers responsible for batch release

For multidose vial
Rovi Pharma Industrial Services, S.A.
Paseo de Europa, 50
28703, San Sebastián de los Reyes
Madrid, Spain

Recipharm Monts
18 Rue de Montbazon
Monts, France 37260

Modern Biotech Spain S.L.
Calle del Príncipe de Vergara 132 Plt 12
Madrid 28002
Spain

For pre-filled syringe
Rovi Pharma Industrial Services, S.A.
Calle Julián Camarillo nº35
28037 Madrid Spain

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

Official batch release

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.
C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

Periodic safety update reports (PSURs)

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

Risk management plan (RMP)

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION

This being a conditional marketing authorisation and pursuant to Article 14-a of Regulation (EC) No 726/2004, the MAH shall complete, within the stated timeframe, the following measures:

<table>
<thead>
<tr>
<th>Description</th>
<th>Due date</th>
</tr>
</thead>
<tbody>
<tr>
<td>In order to confirm the efficacy and safety of Spikevax, the MAH should submit the final Clinical Study Report for the randomised, placebo-controlled, observer-blind study mRNA-1273-P301.</td>
<td>30 June 2023</td>
</tr>
<tr>
<td>In order to confirm the efficacy and safety of Spikevax, the MAH should submit the final Clinical Study Report for the randomised, placebo-controlled, observer-blind study mRNA-1273-P203, including the full bioanalytical report.</td>
<td>31 July 2024</td>
</tr>
<tr>
<td>In order to confirm the efficacy of Spikevax, the MAH should submit the final Clinical Study Report for the randomised, placebo-controlled, observer-blind study mRNA-1273-P204.</td>
<td>31 March 2024</td>
</tr>
</tbody>
</table>
ANNEX III
LABELLING AND PACKAGE LEAFLET
A. LABELLING
PARTICULARS TO APPEAR ON THE OUTER PACKAGING

1. NAME OF THE MEDICINAL PRODUCT

Spikevax 0.2 mg/mL dispersion for injection
COVID-19 mRNA Vaccine (nucleoside modified)
elasomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each multidose vial contains 5 mL.
One dose (0.5 mL) contains 100 micrograms of elasomeran.
One dose (0.25 mL) contains 50 micrograms of elasomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, 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.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 multidose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY
8. **EXPIRY DATE**

EXP

9. **SPECIAL STORAGE CONDITIONS**

Store frozen at -50°C to -15°C. Read the package leaflet for the shelf life after first opening and for additional storage information. Keep the vial in the outer carton to protect from light.

10. **SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

Dispose of in accordance with local requirement.

11. **NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

MODERNA BIOTECH SPAIN, S.L.
Calle del Príncipe de Vergara 132 Plt 12
Madrid 28002
Spain

12. **MARKETING AUTHORISATION NUMBER(S)**

EU/1/20/1507/001

13. **BATCH NUMBER**

Lot

14. **GENERAL CLASSIFICATION FOR SUPPLY**

15. **INSTRUCTIONS ON USE**

16. **INFORMATION IN BRAILLE**

Justification for not including Braille accepted.

17. **UNIQUE IDENTIFIER – 2D BARCODE**

2D barcode carrying the unique identifier included.
<table>
<thead>
<tr>
<th></th>
<th>UNIQUE IDENTIFIER – HUMAN READABLE DATA</th>
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<tbody>
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<tr>
<td>SN</td>
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<td>NN</td>
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<tr>
<td>MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS</td>
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<tr>
<td>---------------------------------------------------------------</td>
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<tr>
<td>MULTIDOSE VIAL LABEL</td>
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<table>
<thead>
<tr>
<th>1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION</th>
</tr>
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<tbody>
<tr>
<td>Spikevax 0.2 mg/mL dispersion for injection</td>
</tr>
<tr>
<td>COVID-19 mRNA Vaccine (nucleoside modified)</td>
</tr>
<tr>
<td>elasomeran</td>
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<td>IM</td>
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<thead>
<tr>
<th>2. METHOD OF ADMINISTRATION</th>
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<tbody>
<tr>
<td>Intramuscular use</td>
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<th>3. EXPIRY DATE</th>
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<th>4. BATCH NUMBER</th>
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<tr>
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<thead>
<tr>
<th>5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT</th>
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</thead>
<tbody>
<tr>
<td>Multidose vial</td>
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<tr>
<td>5 mL</td>
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</table>

<table>
<thead>
<tr>
<th>6. OTHER</th>
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</table>

Scan here for package leaflet or visit [www.modernacovid19global.com](http://www.modernacovid19global.com). Discard date/time:
PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (MULTIDOSE VIAL)

1. **NAME OF THE MEDICINAL PRODUCT**

Spikevax 0.1 mg/mL dispersion for injection
COVID-19 mRNA Vaccine (nucleoside modified)
elasomeran

2. **STATEMENT OF ACTIVE SUBSTANCE(S)**

Each multidose vial contains 2.5 mL. One dose (0.5 mL) contains 50 micrograms of elasomeran.

3. **LIST OF EXCIPIENTS**

Excipients: SM-102, 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.

4. **PHARMACEUTICAL FORM AND CONTENTS**

Dispersion for injection
10 multidose vials

5. **METHOD AND ROUTE(S) OF ADMINISTRATION**

Intramuscular use.
Read the package leaflet before use.

Scan here for package leaflet or visit [www.modernacovid19global.com](http://www.modernacovid19global.com).

6. **SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of sight and reach of children.

7. **OTHER SPECIAL WARNING(S), IF NECESSARY**
8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store frozen at -50°C to -15°C.
Read the package leaflet for the shelf life after first opening and for additional storage information.
Keep the vial in the outer carton to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Dispose of in accordance with local requirement.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
Calle del Príncipe de Vergara 132 Plt 12
Madrid 28002
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.
18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN
### MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

#### MULTIDOSE VIAL LABEL

| 1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION | Spikevax 0.1 mg/mL dispersion for injection  
COVID-19 mRNA Vaccine (nucleoside modified)  
elasomeran  
IM |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2. METHOD OF ADMINISTRATION</td>
<td>Intramuscular use</td>
</tr>
<tr>
<td>3. EXPIRY DATE</td>
<td>EXP</td>
</tr>
<tr>
<td>4. BATCH NUMBER</td>
<td>Lot</td>
</tr>
</tbody>
</table>
| 5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT | Multidose vial  
2.5 mL |
| 6. OTHER | ![QR Code] Scan here for package leaflet or visit [www.modernacovid19global.com](http://www.modernacovid19global.com).  
Discard date/time: |
PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON (PRE-FILLED SYRINGE)

1. NAME OF THE MEDICINAL PRODUCT

Spikevax 50 micrograms dispersion for injection in pre-filled syringe COVID-19 mRNA Vaccine (nucleoside modified) elasomeran

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 0.5 mL. One dose (0.5 mL) contains 50 micrograms of elasomeran.

3. LIST OF EXCIPIENTS

Excipients: SM-102, 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.

4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
10 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.
Single use

Scan here for package leaflet or visit www.modernacovid19global.com.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY
8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store frozen at -50°C to -15°C.
Read the package leaflet for the shelf life and for additional storage information.
Keep the pre-filled syringe in the outer carton to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Dispose of in accordance with local requirement.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MODERNA BIOTECH SPAIN, S.L.
Calle del Príncipe de Vergara 132 Plt 12
Madrid 28002
Spain

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1507/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.
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<thead>
<tr>
<th>PC</th>
<th>SN</th>
<th>NN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>
MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE VIAL LABEL

<table>
<thead>
<tr>
<th>1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spikevax 50 micrograms dispersion for injection</td>
</tr>
<tr>
<td>elasomeran</td>
</tr>
<tr>
<td>IM</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>2. METHOD OF ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intramuscular use</td>
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</tbody>
</table>

<table>
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<tr>
<th>3. EXPIRY DATE</th>
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</thead>
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<td>EXP</td>
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</table>

<table>
<thead>
<tr>
<th>4. BATCH NUMBER</th>
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</thead>
<tbody>
<tr>
<td>Lot</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 mL</td>
</tr>
</tbody>
</table>

| 6. OTHER                                                     |

<table>
<thead>
<tr>
<th>![QR Code]</th>
</tr>
</thead>
</table>
ANNEX III

B. PACKAGE LEAFLET
**Package leaflet: Information for the user**

**Spikevax 0.2 mg/mL dispersion for injection**
**Spikevax 0.1 mg/mL dispersion for injection**
**Spikevax 50 micrograms dispersion for injection in pre-filled syringe**
**COVID-19 mRNA Vaccine (nucleoside modified)**
elasomeran

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

**Read all of this leaflet carefully before you receive this vaccine because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

**What is in this leaflet**
1. What Spikevax is and what it is used for
2. What you need to know before you are given Spikevax
3. How Spikevax is given
4. Possible side effects
5. How to store Spikevax
6. Contents of the pack and other information

1. **What Spikevax is and what it is used for**

Spikevax is a vaccine used to prevent COVID-19 caused by SARS-CoV-2. It is given to adults and children aged 6 years and older. The active substance in Spikevax is mRNA encoding the SARS-CoV-2 Spike protein. The mRNA is embedded in SM-102 lipid nanoparticles.

As Spikevax does not contain the virus, it cannot give you COVID-19.

**How the vaccine works**
Spikevax stimulates the body’s natural defences (immune system). The vaccine works by causing the body to produce protection (antibodies) against the virus that causes COVID-19. Spikevax uses a substance called messenger ribonucleic acid (mRNA) to carry instructions that cells in the body can use to make the spike protein that is also on the virus. The cells then make antibodies against the spike protein to help fight off the virus. This will help to protect you against COVID-19.

2. **What you need to know before you are given Spikevax**

**The vaccine must not be given if** you are allergic to the active substance or any of the other ingredients of this vaccine (listed in section 6).

**Warnings and precautions**
Talk to your doctor, pharmacist or nurse before you are given Spikevax if:

- you have previously had a severe, life-threatening allergic reaction after any other vaccine injection or after you were given Spikevax in the past.
- you have a very weak or compromised immune system
- you have ever fainted following any needle injection.
- you have a bleeding disorder
- you have a high fever or severe infection; however, you can have your vaccination if you have a mild fever or upper airway infection like a cold
- you have any serious illness
- if you have anxiety related to injections

There is an increased risk of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) after vaccination with Spikevax (see section 4).

These conditions can develop within just a few days after vaccination and have primarily occurred within 14 days. They have been observed more often after the second dose compared to the first dose, and more often in younger males.

Following vaccination, you should be alert to signs of myocarditis and pericarditis, such as breathlessness, palpitations and chest pain, and seek immediate medical attention should these occur.

If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before you are given Spikevax.

**Capillary leak syndrome (CLS) flare-ups**
A few cases of capillary leak syndrome flare-ups (causing fluid leakage from small blood vessels (capillaries) resulting in rapid swelling of the arms and legs, sudden weight gain and feeling faint, low blood pressure) have been reported following vaccination with Spikevax. If you have previously had episodes of CLS, talk to a doctor before you are given Spikevax.

**Duration of protection**
As with any vaccine, the primary 2-dose vaccination course of Spikevax may not fully protect all those who receive it and it is not known how long you will be protected.

**Children**
Spikevax is not recommended for children aged under 6 years.

**Other medicines and Spikevax**
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. Spikevax may affect the way other medicines work, and other medicines may affect how Spikevax works.

**Immunocompromised individuals**
If you are immunocompromised, you may receive a third dose of Spikevax. The efficacy of Spikevax even after a third dose may be lower in people who are immunocompromised. In these cases, you should continue to maintain physical precautions to help prevent COVID-19. In addition, your close contacts should be vaccinated as appropriate. Discuss appropriate individual recommendations with your doctor.

**Pregnancy and breast-feeding**
If you are pregnant or think you may be pregnant, tell your doctor, nurse or pharmacist before you receive this vaccine. Spikevax can be used during pregnancy. A large amount of information from pregnant women vaccinated with Spikevax during the second and third trimester have not shown negative effects on the pregnancy or the newborn baby. While information on effects on pregnancy or the newborn baby after vaccination during the first trimester is limited, no change to the risk for miscarriage has been seen.

Spikevax can be given during breastfeeding.
Driving and using machines
Do not drive or use machines if you are feeling unwell after vaccination. Wait until any effects of the vaccine have worn off before you drive or use machines.

Spikevax contains sodium
This medicine contains less than 1 mmol (23 mg) sodium per dose and, that is to say, essentially ‘sodium-free’.

3. How you will be given Spikevax

Table 1. Spikevax dosing for primary series, a third dose in severely immunocompromised and booster doses

<table>
<thead>
<tr>
<th>Vaccination</th>
<th>Spikevax 0.2 mg/mL dispersion for injection</th>
<th>Spikevax 0.1 mg/mL dispersion for injection and Spikevax 50 micrograms dispersion for injection in pre-filled syringe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary series</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>It is recommended to get the second dose of the same vaccine 28 days after the first dose to complete the vaccination course.</td>
<td>Individuals 12 years of age and older two 0.5 mL injections</td>
<td>Not applicable*</td>
</tr>
<tr>
<td></td>
<td>Children 6 through 11 years of age two 0.25 mL injections</td>
<td>Children 6 through 11 years of age two 0.5 mL injections</td>
</tr>
<tr>
<td><strong>Third dose in severely immunocompromised individuals</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>at least 1 month after the second dose</td>
<td>Individuals 12 years of age and older 0.5 mL</td>
<td>Not applicable†</td>
</tr>
<tr>
<td></td>
<td>Children 6 through 11 years of age 0.25 mL</td>
<td>Children 6 through 11 years of age 0.5 mL</td>
</tr>
<tr>
<td><strong>Booster dose</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>may be given at least 3 months after the second dose</td>
<td>Individuals 12 years of age and older 0.25 mL</td>
<td>Individuals 12 years of age and older 0.5 mL</td>
</tr>
</tbody>
</table>

*For primary series for individuals 12 years of age and older, the 0.2 mg/mL strength vial should be used.
†For the third dose in severely immunocompromised patients 12 years of age and older, the 0.2 mg/mL strength vial should be used.

If you miss an appointment for your primary 2nd dose of Spikevax
- If you miss an appointment, arrange another visit as soon as possible with your doctor, pharmacist or nurse.
- If you miss a scheduled injection, you may not be fully protected against COVID-19.

Your doctor, pharmacist or nurse will inject the vaccine into a muscle (intramuscular injection) in your upper arm.

After each injection of the vaccine, your doctor, pharmacist or nurse will watch over you for at least 15 minutes to monitor for signs of an allergic reaction.

If you have any further questions on the use of this vaccine, ask your doctor, pharmacist or nurse.
4. Possible side effects

Like all medicines, this vaccine can cause side effects, although not everybody gets them.

Get **urgent** medical attention if you get any of the following signs and symptoms of an allergic reaction:
- feeling faint or light-headed;
- changes in your heartbeat;
- shortness of breath;
- wheezing;
- swelling of your lips, face, or throat;
- hives or rash;
- nausea or vomiting;
- stomach pain.

Talk to your doctor or nurse if you develop any other side effects. These can include:

**Very common** (may affect more than 1 in 10 people):
- swelling/tenderness in the underarm
- headache
- nausea
- vomiting
- muscle ache, joint aches, and stiffness
- pain or swelling at the injection site
- redness at the injection site (some of which may occur approximately 9 to 11 days after the injection)
- feeling very tired
- chills
- fever

**Common** (may affect up to 1 in 10 people):
- diarrhoea
- rash
- rash or hives at the injection site (some of which may occur approximately 9 to 11 days after the injection)

**Uncommon** (may affect up to 1 in 100 people):
- itchiness at the injection site
- dizziness
- stomach pain

**Rare** (may affect up to 1 in 1 000 people)
- temporary one-sided facial drooping (Bell’s palsy)
- swelling of the face (swelling of the face may occur in patients who have had facial cosmetic injections.)
- decreased sense of touch or sensation
- unusual feeling in the skin, such as tingling or a crawling feeling (paraesthesia)

**Very rare** (may affect up to 1 in 10 000 people)
- inflammation of the heart muscle (myocarditis) or inflammation of the lining outside the heart (pericarditis) which can result in breathlessness, palpitations or chest pain

**Frequency unknown**
- severe allergic reactions with breathing difficulties (anaphylaxis)
- reaction of increased sensitivity or intolerance by the immune system (hypersensitivity)
- a skin reaction that causes red spots or patches on the skin that may look like a target or “bulls-eye” with a dark red centre surrounded by paler red rings (erythema multiforme)
- extensive swelling of the vaccinated limb

**Reporting of side effects**
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this vaccine.

**5. How to store Spikevax**

Keep this vaccine out of the sight and reach of children.

Do not use this vaccine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Information about storage, expiry, and use and handling are described in the section intended for healthcare professionals at the end of the package leaflet.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

**6. Contents of the pack and other information**

**What Spikevax contains**

**Table 2. Composition by container type**

<table>
<thead>
<tr>
<th>Strength</th>
<th>Container</th>
<th>Dose(s)</th>
<th>Composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spikevax 0.2 mg/mL dispersion for injection</td>
<td>Multidose vial</td>
<td>Maximum 10 doses of 0.5 mL each</td>
<td>One dose (0.5 mL) contains 100 micrograms of elasomeran, a COVID-19 mRNA Vaccine (embedded in SM-102 lipid nanoparticles).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maximum 20 doses of 0.25 mL each</td>
<td>One dose (0.25 mL) contains 50 micrograms of elasomeran, a COVID-19 mRNA Vaccine (embedded in SM-102 lipid nanoparticles).</td>
</tr>
<tr>
<td>Spikevax 0.1 mg/mL dispersion for injection and Spikevax 50 micrograms dispersion for injection in pre-filled syringe</td>
<td>Multidose vial</td>
<td>5 doses of 0.5 mL each</td>
<td>One dose (0.5 mL) contains 50 micrograms of elasomeran, a COVID-19 mRNA Vaccine (embedded in SM-102 lipid nanoparticles).</td>
</tr>
<tr>
<td>Pre-filled syringe</td>
<td>1 dose of 0.5 mL</td>
<td>One dose (0.5 mL) contains 50 micrograms of elasomeran, a COVID-19 mRNA Vaccine (embedded in SM-102 lipid nanoparticles).</td>
<td></td>
</tr>
<tr>
<td>--------------------</td>
<td>-----------------</td>
<td>------------------------------------------------------------------</td>
<td></td>
</tr>
</tbody>
</table>

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.

The other ingredients are 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.

**What Spikevax looks like and contents of the pack**

**Spikevax 0.2 mg/mL dispersion for injection**

Spikevax is a white to off white dispersion supplied in a 5 mL glass vial with a rubber stopper and red flip-off plastic cap with aluminium seal.

Pack size: 10 multidose vials

**Spikevax 0.1 mg/mL dispersion for injection**

Spikevax is a white to off white dispersion supplied in a 2.5 mL glass vial with a rubber stopper and blue flip-off plastic cap with aluminium seal.

Pack size: 10 multidose vials

**Spikevax 50 micrograms dispersion for injection in pre-filled syringe**

Spikevax is a white to off white dispersion supplied in a pre-filled syringe (polymeric) with plunger stopper and a tip cap (without needle).

The pre-filled syringe is packaged in 5 clear blisters containing 2 pre-filled syringes in each blister.

Pack size: 10 pre-filled syringes

**Marketing Authorisation Holder**
MODERNA BIOTECH SPAIN, S.L.
Calle del Príncipe de Vergara 132 Plt 12
Madrid 28002
Spain

**Manufacturer**

For multidose vials

Rovi Pharma Industrial Services, S.A.
Paseo de Europa, 50
28703. San Sebastián de los Reyes
Madrid, Spain

Recipharm Monts
18 Rue de Montbazon  
Monts, France 37260

Moderna Biotech Spain S.L.  
Calle del Príncipe de Vergara 132 Plt 12  
Madrid 28002  
Spain

For pre-filled syringe

Rovi Pharma Industrial Services, S.A.  
Calle Julián Camarillo n°35  
28037 Madrid Spain

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

<table>
<thead>
<tr>
<th>Country</th>
<th>Tel/Tel:</th>
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</thead>
<tbody>
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<td>0800 81 460</td>
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<tr>
<td>България</td>
<td>00800 115 4477</td>
</tr>
<tr>
<td>Česká republika</td>
<td>800 050 719</td>
</tr>
<tr>
<td>Danmark</td>
<td>80 81 06 53</td>
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<tr>
<td>Deutschland</td>
<td>0800 100 9632</td>
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<td>Eesti</td>
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<td>Elλάδα</td>
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<td>Italia</td>
<td>800 928 007</td>
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<td>0800 400 625</td>
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<td>Slovenija</td>
<td>080 083082</td>
</tr>
<tr>
<td>Slovenská republika</td>
<td>0800 191 647</td>
</tr>
<tr>
<td>Suomi/Finland</td>
<td>0800 774198</td>
</tr>
<tr>
<td>Sverige</td>
<td></td>
</tr>
</tbody>
</table>
This leaflet was last revised in

This vaccine has been given ‘conditional approval’. This means that there is more evidence to come about this vaccine.

The European Medicines Agency will review new information on this vaccine at least every year and this leaflet will be updated as necessary.

Scan the code with a mobile device to get the package leaflet in different languages.


This leaflet is available in all EU/EEA languages on the European Medicines Agency website.

------------------------------------------------------------------------------------------------------------------------

The following information is intended for healthcare professionals only:

**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.

**Storage and preparation for administration**

Spikevax should be administered by a trained healthcare professional.

The vaccine comes ready to use once thawed.

Do not shake or dilute.

The vaccine should be inspected visually for particulate matter and discoloration prior to administration.

Spikevax is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discoloured or contains other particulate matter.

Thawed vials and pre-filled syringes can be handled in room light conditions.
Spikevax 0.2 mg/mL dispersion for injection (multidose vials with a red flip-off cap)

Ten (10) doses (of 0.5 mL each) or a maximum of twenty (20) doses (of 0.25 mL each) can be withdrawn from each multidose vial.

Pierce the stopper preferably at a different site each time. Do not puncture the red-cap vial more than 20 times.

Spikevax 0.1 mg/mL dispersion for injection (multidose vials with a blue flip-off cap)

Five (5) doses (of 0.5 mL each) can be withdrawn from each multidose vial.

Pierce the stopper preferably at a different site each time.
**Spikevax 50 micrograms dispersion for injection in pre-filled syringe**

Do not shake or dilute the contents of the pre-filled syringe.

Each pre-filled syringe is for single use only. The vaccine comes ready to use once thawed.

One (1) dose of 0.5 mL can be administered from each pre-filled syringe.

Spikevax is supplied in a single-dose, pre-filled syringe (without needle) containing 0.5 mL (50 micrograms) mRNA and must be thawed prior to administration.

During storage, minimise exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

Thaw each pre-filled syringe before use following the instructions below. Syringes may be thawed in the blister packs (each blister containing 2 pre-filled syringes) or in the carton itself, either in the refrigerator or at room temperature (Table 3).
Table 3. Thawing instructions for pre-filled syringes and cartons before use

<table>
<thead>
<tr>
<th>Configuration</th>
<th>Thaw Temperature (in a refrigerator) °C</th>
<th>Thaw Duration (mins)</th>
<th>Thaw Temperature (at room temperature) °C</th>
<th>Thaw Duration (mins)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-filled syringe in blister pack</td>
<td>2 – 8</td>
<td>55</td>
<td>15 – 25</td>
<td>45</td>
</tr>
<tr>
<td>Carton</td>
<td>2 – 8</td>
<td>155</td>
<td>15 – 25</td>
<td>140</td>
</tr>
</tbody>
</table>

Handling instructions for the pre-filled syringes
- Let each pre-filled syringe stand at room temperature (15°C to 25°C) for 15 minutes before administering.
- Do not shake.
- Pre-filled syringe should be inspected visually for particulate matter and discoloration prior to administration.
- Spikevax is a white to off-white dispersion. It may contain white or translucent product-related particulates. Do not administer if vaccine is discolored or contains other particulate matter.
- Needles are not included in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner needles).
- Remove tip cap from syringe by twisting in a counter-clockwise direction.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe.
- Uncap the needle when ready for administration.
- Administer the entire dose intramuscularly.
- After thawing, do not refreeze.
- Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Dosing and schedule

Table 4. Spikevax dosing for primary series, a third dose in severely immunocompromised and booster doses

<table>
<thead>
<tr>
<th>Vaccination</th>
<th>Spikevax 0.2 mg/mL dispersion for injection</th>
<th>Spikevax 0.1 mg/mL dispersion for injection and Spikevax 50 micrograms dispersion for injection in pre-filled syringe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary series</td>
<td>Individuals 12 years of age and older two 0.5 mL injections</td>
<td>Not applicable*</td>
</tr>
<tr>
<td></td>
<td>Children 6 through 11 years of age two 0.25 mL injections</td>
<td>Children 6 through 11 years of age two 0.5 mL injections</td>
</tr>
<tr>
<td>Vaccination</td>
<td>Spikevax 0.2 mg/mL dispersion for injection</td>
<td>Spikevax 0.1 mg/mL dispersion for injection and Spikevax 50 micrograms dispersion for injection in pre-filled syringe</td>
</tr>
<tr>
<td>----------------------------------------------------------------------------</td>
<td>---------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Third dose in severely immunocompromised</strong> at least 1 month after the second dose</td>
<td>Individuals 12 years of age and older 0.5 mL</td>
<td>Not applicable†</td>
</tr>
<tr>
<td></td>
<td>Children 6 through 11 years of age 0.25 mL</td>
<td>Children 6 through 11 years of age 0.5 mL</td>
</tr>
<tr>
<td><strong>Booster dose</strong> may be given at least 3 months after the second dose</td>
<td>Individuals 12 years of age and older 0.25 mL</td>
<td>Individuals 12 years of age and older 0.5 mL</td>
</tr>
</tbody>
</table>

*For primary series for individuals 12 years of age and older, the 0.2 mg/mL strength vial should be used.
†For the third dose in severely immunocompromised patients 12 years of age and older, the 0.2 mg/mL strength vial should be used.

As with all injectable vaccines, appropriate medical treatment and supervision must always be readily available in the event of an anaphylactic reaction following the administration of Spikevax.

Individuals should be observed by a healthcare professional for at least 15 minutes after vaccination.

There are no data to assess the concomitant administration of Spikevax with other vaccines. Spikevax must not be mixed with other vaccines or medicinal products in the same syringe.

**Administration**

The vaccine must be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm. Do not administer this vaccine intravascularly, subcutaneously or intradermally.

**Multidose vials**
Pre-filled syringes
Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner). Remove tip cap from pre-filled syringe by twisting in a counter-clockwise direction. Attach the needle by twisting in a clockwise direction until the needle fits securely on the syringe. Uncap the needle when ready for administration. Administer the entire dose intramuscularly. Discard syringe after use. For single-use only.
Annex IV
Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)
Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for elasomeran, the scientific conclusions of CHMP are as follows:

**Extensive swelling of vaccinated limb**

In view of available data on Extensive swelling of vaccinated limb, including a high number of spontaneous reports with a close temporal relationship, and in view of a plausible mechanism of action, the PRAC considers that a causal relationship between elasomeran and extensive swelling of vaccinated limb is at least a reasonable possibility. The PRAC concluded that the product information of products containing elasomeran should be amended accordingly.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for elasomeran the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing elasomeran is unchanged subject to the proposed changes to the product information

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.