# 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

mCOMBRIAX dispersion for injection in pre-filled syringe

Influenza and COVID-19, mRNA vaccine

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each single-use pre-filled syringe contains one dose of 0.32 mL.

One dose (0.32 mL) contains 31.7 micrograms of total RNA.

mCOMBRIAX is single-stranded, 5'-capped messenger RNAs (mRNAs) produced using a cell-free in vitro transcription from the corresponding DNA template, encoding seasonal influenza haemagglutinin (HA) glycoproteins: A/H1N1, A/H3N2, B/Victoria, and the linked N-terminal domain and receptor-binding domain of the viral spike (S) protein of SARS-CoV-2.

Influenza virus strains and SARS-CoV-2 composition per 0.32 mL dose:

A/Wisconsin/67/2022 (A/H1N1)pdm09 .....8.3 micrograms RNA
A/Darwin/6/2021 (A/H3N2) .....8.3 micrograms RNA
B/Austria/1359417/2021 (B/Victoria lineage) .....8.3 micrograms RNA
SARS-CoV-2 Omicron XBB.1.5 .....6.7 micrograms RNA

This vaccine complies with the World Health Organisation (WHO) recommendations (Northern Hemisphere) and EU recommendations for the 2023/2024 season.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Dispersion for injection

White to off-white dispersion (pH: 7.1 – 7.8).

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

mCOMBRIAX is indicated for active immunisation for the prevention of influenza disease and COVID-19 caused by SARS-CoV-2 in individuals 50 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

*Adults 50 years of age and older*

One dose of 0.32 mL.

If previously vaccinated with a COVID-19 vaccine, this vaccine should be administered at least 3 months after the most recent dose of a COVID-19 vaccine (see sections 4.4 and 5.1).

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

*Paediatric population*
The safety and efficacy of mCOMBRIAX in children less than 18 years of age have not yet been established. No data are available.

Method of administration

For intramuscular injection only.

This vaccine should be administered preferably in the deltoid muscle of the upper arm.

The vaccine must not be injected intravenously, subcutaneously or intradermally.

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

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

For instructions on preparation of the medicinal product before administration, see section 6.6.

## 4.3 Contraindications

Hypersensitivity to the active substances 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

Appropriate medical treatment and supervision should always be readily available in case of severe hypersensitivity reaction, including anaphylaxis following administration of the vaccine. Close observation for at least 15 minutes is recommended following vaccination. No further dose of the vaccine should be given to those who have experienced anaphylaxis after a prior dose of the vaccine.

Myocarditis and pericarditis

An increased risk of myocarditis and pericarditis has been observed following vaccination with some other COVID-19 vaccines. These conditions can develop within a few days and primarily occurred within 14 days. They have been observed more often in younger males.

Healthcare professionals should be alert to the signs and symptoms of myocarditis and pericarditis. Vaccine recipients (including caregivers) should be instructed to seek immediate medical attention if they develop symptoms indicative of myocarditis or pericarditis.

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

Safety and immunogenicity data on this vaccine are not available for immunocompromised individuals. Individuals receiving immunosuppressant therapy or patients with immunodeficiency may have a diminished immune response to this vaccine.

Limitations of vaccine effectiveness

As with all vaccines, vaccination with mCOMBRIAX may not protect all vaccine recipients.

Duration of protection

The duration of protection afforded by the vaccine is unknown.

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

No interaction studies with other medicinal products have been performed. Concomitant administration of mCOMBRIAX with other vaccines has not been studied.

## 4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of mCOMBRIAX in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of mCOMBRIAX during pregnancy.

Breast-feeding

No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to mCOMBRIAX active substances is negligible. mCOMBRIAX can be used during breast-feeding.

Fertility

No human data on the effect of mCOMBRIAX on fertility are available.

Animal studies do not indicate direct or indirect harmful effects with respect to female reproductive toxicity. Animal studies conducted with the vaccine are insufficient to assess functional effects on male reproductive toxicity (see section 5.3).

## 4.7 Effects on ability to drive and use machines

mCOMBRIAX has no or negligible influence on the ability to drive and use machines. However, some of the effects mentioned under section 4.8 (e.g., fatigue) may temporarily affect the ability to drive or use machines.

## 4.8 Undesirable effects

Data for Quadrivalent Influenza and COVID-19 mRNA Combination Vaccine are relevant to mCOMBRIAX because both vaccines are manufactured using the same process and have overlapping compositions.

Summary of the safety profile

The most commonly reported adverse reactions were injection site pain (75.8%), fatigue (55.9%), myalgia (54.8%), headache (47.5%), arthralgia (44.6%), chills (38.2%), lymphadenopathy (22.5%), nausea/vomiting (15.7%) and pyrexia (13.2%). The median time to onset for solicited adverse reactions was Day 2, with median duration of 3 days.

Tabulated list of adverse reactions

The safety of mCOMBRIAX was evaluated in a Phase 3 clinical study in which 4 004 participants aged 50 years and older received Quadrivalent Influenza and COVID-19, mRNA Combination Vaccine (see section 5.1). The median duration of follow-up was 171 days.

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 frequency (Table 1).

**Table 1. Adverse reactions**

| MedDRA system organ class | Frequency | Adverse reaction |
|---|---|---|
| Blood and lymphatic system disorders | Very common | Lymphadenopathy* |
| Nervous system disorders | Very common | Headache |
| Gastrointestinal disorders | Very common | Nausea/vomiting |
| | Uncommon | Diarrhoea |
| Musculoskeletal and connective tissue disorders | Very common | Myalgia<br>Arthralgia |
| General disorders and administration site conditions | Very common | Injection site pain<br>Fatigue<br>Chills<br>Pyrexia |
| | Common | Injection site swelling<br>Injection site erythema |
| | Uncommon | Injection site pruritus |

* Lymphadenopathy included mainly axillary (underarm) swelling or tenderness ipsilateral to the side of injection and other associated terms including lymphadenitis, lymph node pain, and lymph node involvement in other locations (e.g., cervical, supraclavicular).

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.

### 4.9 Overdose

In case of overdose, it is recommended that the individual be monitored for any signs or symptoms of adverse reactions or effects and appropriate symptomatic treatment instituted immediately.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: not yet assigned, ATC code: not yet assigned

Mechanism of action

mCOMBRIAX is a nucleoside-modified mRNA-based vaccine formulated in lipid nanoparticles encoding influenza and SARS-CoV-2 antigens. The influenza antigens encoded are the full-length, membrane-bound HA glycoproteins of seasonal influenza virus types A (H1N1 and H3N2) and B (Victoria lineage). The SARS-CoV-2 antigen encoded is the membrane-bound, linked N-terminal domain (NTD) and receptor-binding domain (RBD) of the spike (S) glycoprotein from SARS-CoV-2 strains.

After delivery into cells, the mRNA serves as a template for the synthesis of the intended proteins. The vaccine elicits immune responses to the HA antigens and NTD-RBD of the S antigen, which contribute to protection against influenza and COVID-19.

Immunogenicity

Data for Quadrivalent Influenza and COVID-19 mRNA Combination Vaccine are relevant to mCOMBRIAX because both vaccines are manufactured using the same process and have overlapping compositions.

Study 1 is a Phase 3, randomised, stratified, observer-blind, active-control study conducted in two age groups (Cohort A and Cohort B) to evaluate the safety, reactogenicity and immunogenicity of Quadrivalent Influenza and COVID-19, mRNA Combination Vaccine in adults ≥50 years of age.

The per-protocol immunogenicity set (PPIS) for Cohort A included participants ≥65 years of age who received Quadrivalent Influenza and COVID-19, mRNA Combination Vaccine and placebo (referred to as the mCOMBRIAX group; N=1 886) or coadministration of licensed high-dose quadrivalent influenza vaccine (HD-IIV4) and COVID-19 mRNA vaccine (referred to as the Comparator A group; N=1 883). The median age of participants was 70.0 years, 20.6% were aged ≥75 years, 54.2% were female, 78.5% identified as White, 18.4% as Black or African American, and 13.9% as Hispanic or Latino. A total of 50.7% of participants had received an influenza vaccine and 42.4% had received a COVID-19 vaccine in the season prior to study enrolment.

The PPIS for Cohort B included participants aged 50 to 64 years who received Quadrivalent Influenza and COVID-19, mRNA Combination Vaccine and placebo (referred to as the mCOMBRIAX group; N=1 890) or coadministration of licensed standard dose quadrivalent influenza vaccine (SD-IIV4) and COVID-19 mRNA vaccine (referred to as the Comparator B group; N=1 884). The median age was 58.0 years, 59.0% of participants were female, 67.9% identified as White, 26.6% as Black or African

American, and 19.6% as Hispanic or Latino. A total of 39.4% of participants had received an influenza vaccine and 31.0% had received a COVID-19 vaccine in the season prior to study enrolment.

The primary immunogenicity objective was to demonstrate non-inferiority of immune response induced by mCOMBRIAX versus active comparators against vaccine-matched influenza strains and SARS-CoV-2 at Day 29 after vaccination based on haemagglutination inhibition (HAI) geometric mean titre (GMT) ratios and seroconversion rate (SCR) differences for the 4 influenza strains and pseudovirus neutralisation assay (PsVNA) geometric mean concentration (GMC) ratio and seroresponse rate (SRR) difference for SARS-CoV-2.

Non-inferiority was defined as lower bound of 2-sided 97.5% confidence interval (CI) of the geometric mean ratios (GMRs) being >0.667 and for the SCR/SRR differences being >-10% for all 4 influenza strains and the SARS-CoV-2 variant. mCOMBRIAX met non-inferiority criteria for all influenza strains and for SARS-CoV-2 compared to Comparator A among participants ≥65 years and compared to Comparator B among participants 50 to 64 years (Table 2).

**Table 2. Study 1: Immunogenicity Results in participants ≥50 years (PPIS)**

| **Virus** | **GM level[a] (95% CI)** | | **GMR[a] (97.5% CI)** | **SCR (for influenza) or SRR (for SARS-CoV-2)[b] (95% CI)** | | **SCR/SRR difference n (%)[b] (97.5% CI)** |
|---|---|---|---|---|---|---|
| **In participants ≥65 years of age (Cohort A)[c]** | | | | | | |
| | **mCOMBRIAX N=1 886** | **Comparator A N=1 883** | **mCOMBRIAX versus Comparator A** | **mCOMBRIAX N=1 886** | **Comparator A N=1 883** | **mCOMBRIAX versus Comparator A** |
| **Influenza A/H1N1[d]** | 120.5 (116.0, 125.2) | 104.3 (100.4, 108.4) | 1.155 (1.086, 1.229) | 36.4 (34.3, 38.7) | 31.1 (29.0, 33.2) | 5.4 (1.9, 8.8) |
| **Influenza A/H3N2[d]** | 114.7 (110.4, 119.1) | 107.9 (103.9, 112.1) | 1.063 (0.999, 1.130) | 38.7 (36.5, 40.9) | 34.6 (32.5, 36.8) | 4.0 (0.5, 7.6) |
| **Influenza B/Victoria[d]** | 245.3 (237.8, 252.9) | 219.4 (212.8, 226.3) | 1.118 (1.063, 1.175) | 23.9 (22.0, 25.9) | 19.4 (17.6, 21.2) | 4.5 (1.5, 7.5) |
| **Influenza B/Yamagata** | 93.3 (91.1, 95.6) | 92.6 (90.4, 94.9) | 1.007 (0.969, 1.047) | 8.8 (7.5, 10.1) | 10.2 (8.9, 11.7) | -1.4 (-3.6, 0.7) |
| **SARS-CoV-2 (Omicron XBB.1.5)[d]** | 1396.7 (1326.6, 1470.5) | 851.1 (808.6, 895.9) | 1.641 (1.510, 1.783) | 82.3 (80.5, 84.1) | 69.6 (67.4, 71.7) | 12.8 (9.6, 15.9) |
| **In participants 50 to 64 years of age (Cohort B)[c]** | | | | | | |
| | **mCOMBRIAX N=1 890** | **Comparator B N=1 884** | **mCOMBRIAX versus Comparator B** | **mCOMBRIAX N=1 890** | **Comparator B N=1 884** | **mCOMBRIAX versus Comparator B** |
| **Influenza A/H1N1[d]** | 137.7 (132.1, 143.5) | 97.3 (93.4, 101.5) | 1.414 (1.322, 1.513) | 50.6 (48.3, 52.9) | 32.7 (30.6, 34.8) | 17.9 (14.3, 21.4) |
| **Influenza A/H3N2[d]** | 111.5 (107.5, 115.7) | 80.8 (77.9, 83.8) | 1.380 (1.300, 1.465) | 41.9 (39.7, 44.2) | 27.4 (25.4, 29.5) | 14.6 (11.1, 18.0) |
| **Influenza B/Victoria[d]** | 224.9 (218.0, 232.0) | 185.0 (179.3, 190.8) | 1.216 (1.156, 1.278) | 25.8 (23.9, 27.9) | 17.2 (15.5, 19.0) | 8.6 (5.6, 11.6) |
| **Influenza B/Yamagata[d]** | 101.7 (99.3, 104.3) | 88.1 (86.0, 90.3) | 1.154 (1.109, 1.201) | 13.0 (11.5, 14.6) | 10.3 (9.0, 11.8) | 2.7 (0.3, 5.0) |
| **SARS-CoV-2 (Omicron XBB.1.5)[d]** | 1551.6 (1476.3, 1630.7) | 1186.1 (1128.5, 1246.7) | 1.308 (1.207, 1.418) | 84.6 (82.8, 86.2) | 76.5 (74.5, 78.4) | 8.1 (5.2, 11.0) |

CI=confidence interval; GMR=geometric mean ratio; GM=geometric mean; HA=haemagglutinin; HAI=haemagglutination inhibition; LLOQ=lower limit of quantification; nAb=neutralizing antibody; PsVNA=pseudovirus neutralization assay; SARS-CoV-2=severe acute respiratory syndrome coronavirus 2; SCR=seroconversion rate; SRR=seroresponse rate.
Comparator A: licensed HD-IIV4 and COVID-19 mRNA vaccines.
Comparator B: licensed SD-IIV4 and COVID-19 mRNA vaccines.
[a] The model-based GM level and GMR are from analysis of covariance model with vaccination group as the fixed variable, adjusting for the randomisation stratification factors and baseline antibody level.
[b] Seroconversion was defined as a Day 29 post-injection level ≥1:40 if baseline was <1:10 or a ≥4-fold rise if baseline was ≥1:10 in anti HA antibodies measured by the HAI assay. Seroresponse was defined as a Day 29 post-injection level ≥4-fold rise if baseline was ≥LLOQ or ≥4×LLOQ if baseline value was <LLOQ in the nAb values measured by PsVNA.
[c] The study enrolled adults at increased risk for severe influenza and/or COVID-19 comprising approximately 65% of Cohort A and 62% of Cohort B.
[d] Secondary immunogenicity superiority (pre-specified) criteria (2-sided 95% CI lower bound: GMR >1; SCR/SRR difference >0%) were met for all vaccine-matched strains, except for B/Yamagata in Cohort A.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with mCOMBRIAX in one or more subsets of the paediatric population in active immunisation to prevent influenza and COVID-19 caused by SARS-CoV-2 (see section 4.2 for information on paediatric use).

### 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 repeated dose toxicity, genotoxicity, toxicity to reproduction and development.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate (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
Sucrose
Water for injections

### 6.2 Incompatibilities

In the absence of compatibility studies, this vaccine must not be mixed with other medicinal products.

### 6.3 Shelf life

1 year at -40 °C to -15 °C.

Within the shelf life of 1 year, the vaccine is stable for 30 days when stored at 2 °C to 8 °C and protected from light. At the end of 30 days, the vaccine should be used immediately or discarded (see section 6.4).

Once thawed, the vaccine should not be refrozen.

Upon moving the vaccine to 2 °C to 8 °C storage, the outer carton should be marked with the new expiry date at 2 °C to 8 °C.

The pre-filled syringes may be stored at 8 °C to 25 °C for up to 24 hours after removal from refrigerated conditions. Within this period of time, pre-filled syringes may be handled in ambient light conditions. Do not refrigerate after being stored at 8 °C to 25 °C. Discard the syringe if not used within this time.

## 6.4 Special precautions for storage

Store in a freezer at -40 °C to -15 °C.

Once thawed, store in a refrigerator (2 °C to 8 °C) and do not refreeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.

After thawing, pre-filled syringes may be stored refrigerated between 2 °C to 8 °C for up to 30 days prior to use.

Transportation of thawed pre-filled syringes

Thawed pre-filled syringes can be transported at 2 °C to 8 °C using shipping containers which have been qualified to maintain 2 °C to 8 °C. Once thawed and transported 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 (see section 6.3).

## 6.5 Nature and contents of container

0.32 mL of dispersion in a pre-filled syringe (cyclic olefin copolymer) with halobutyl plunger stopper and halobutyl rubber tip cap in rigid plastic cover (without needle).

The pre-filled syringes are packaged in a paper inner tray within a carton containing 1 or 10 pre-filled syringes.

Not all pack sizes may be marketed.

## 6.6 Special precautions for disposal and other handling

Handling instructions before use

The vaccine is ready to use once thawed.

Do not dilute the product.

Do not shake the pre-filled syringe before use.

The pre-filled syringe is for single-use only.

Do not use if the pre-filled syringe has been dropped or damaged or the security seal on the carton has been broken.

mCOMBRIAX is shipped and supplied either as a frozen or thawed pre-filled syringe (see section 6.4). If the vaccine is frozen, it must be completely thawed before use. Thaw each pre-filled syringe before use, either in the refrigerator or at room temperature, following the instructions in Table 3.

Prior to immediate use, single syringe may be removed from a carton of 1 or 10 pre-filled syringes and thawed either in the refrigerator or at room temperature. The remaining syringes must continue to be stored in their original carton in the freezer or refrigerator.

**Table 32. Thawing instructions for pre-filled syringes and cartons before use**

| Configuration | Thaw Instructions and Durations | | | |
|---|---|---|---|---|
| | **Thaw temperature (in a refrigerator) (°C)** | **Thaw duration (minutes)** | **Thaw temperature (at room temperature) (°C)** | **Thaw duration (minutes)** |
| One pre-filled syringe or a carton of 1 pre-filled syringe | 2 – 8 | 100 | 15 – 25 | 40 |
| Carton of 10 pre-filled syringes | 2 – 8 | 160 | 15 – 25 | 80 |

- After thawing, the vaccine cannot be re-frozen.
- If the vaccine has been thawed at room temperature (15 °C to 25 °C), the pre-filled syringe is ready to administer. Syringes should not be returned to the refrigerator after being thawed at room temperature.
- The pre-filled syringes may be stored at 8 °C to 25 °C for a total of 24 hours after removal from refrigerated conditions. Discard the thawed pre-filled syringe if not used within this time.

Administration

- Remove a pre-filled syringe from the outer carton.
- The pre-filled syringe should be inspected visually for particulate matter and discolouration prior to administration.
- Do not administer if vaccine is discoloured or contains other particulate matter.
- Needles are not provided in the pre-filled syringe cartons.
- Use a sterile needle of the appropriate size for intramuscular injection (21-gauge or thinner needles).
- With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the pre-filled syringe.
- Uncap the needle when ready for administration.
- The vaccine should be administered immediately after uncapping.
- Administer the entire dose intramuscularly.
- Discard the pre-filled syringe after single use.

Disposal

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.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

## 8. MARKETING AUTHORISATION NUMBER(S)

EU/1/26/2028/001
EU/1/26/2028/002

## 9. DATE OF FIRST AUTHORISATION

Date of first authorisation:

## 10. DATE OF REVISION OF THE TEXT

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

# ANNEX II

**A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**

**B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**

**C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

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

## A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance(s)

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

Name and address of the manufacturer responsible for batch release

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo n° 31
28037 Madrid
Spain

## 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.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

## 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.

**ANNEX III**

**LABELLING AND PACKAGE LEAFLET**

# A. LABELLING

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**OUTER CARTON**

## 1. NAME OF THE MEDICINAL PRODUCT

mCOMBRIAX dispersion for injection in pre-filled syringe
Influenza and COVID-19, mRNA Vaccine

## 2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains one dose of 0.32 mL. One dose contains 8.3 micrograms of haemagglutinin RNA per influenza virus strain and 6.7 micrograms of SARS-CoV-2 RNA.

## 3. LIST OF EXCIPIENTS

Excipients: 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, sucrose, water for injections.

See leaflet for further information.

## 4. PHARMACEUTICAL FORM AND CONTENTS

Dispersion for injection
1 pre-filled syringe
10 pre-filled syringes

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

Intramuscular use.
For single use only.
Read the package leaflet before use.

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

Keep out of the sight and reach of children.

## 7. OTHER SPECIAL WARNING(S), IF NECESSARY

## 8. EXPIRY DATE

EXP (-40 °C to -15 °C)
EXP (2 °C to 8 °C)

## 9. SPECIAL STORAGE CONDITIONS

Store in a freezer (-40 ºC to -15 ºC).
Keep the pre-filled syringe in the outer carton in order to protect from light.

For additional information on shelf-life and storage, see the package leaflet.

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

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

MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

## 12. MARKETING AUTHORISATION NUMBER(S)

EU/1/26/2028/001 1 pre-filled syringe in a tray
EU/1/26/2028/002 10 pre-filled syringes in a tray

## 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**

**PRE-FILLED SYRINGE LABEL**

## 1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

mCOMBRIAX dispersion for injection
Influenza and COVID-19, mRNA Vaccine
IM

## 2. METHOD OF ADMINISTRATION

Intramuscular use

## 3. EXPIRY DATE

EXP

## 4. BATCH NUMBER

Lot

## 5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.32 mL

## 6. OTHER

**B. PACKAGE LEAFLET**

**Package leaflet: Information for the user**

**mCOMBRIAX dispersion for injection in pre-filled syringe**
Influenza and COVID-19, mRNA Vaccine

▼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 mCOMBRIAX is and what it is used for

mCOMBRIAX is a vaccine that helps to protect adults aged 50 years and older against flu (influenza) and COVID-19 caused by SARS-CoV-2.

The active substances in mCOMBRIAX are molecules called messenger ribonucleic acid (mRNA). The mRNA provides instructions for making parts of the spike protein (a protein on the surface of SARS-CoV-2 that the virus needs to enter the body's cells) and glycoproteins (proteins on the surface of type A and type B influenza viruses that help the viruses enter the cells and spread in the body).

When a person is given mCOMBRIAX, some of their cells will read the mRNA instructions and temporarily produce parts of the spike protein and glycoproteins. The person's immune system (the body's natural defence system) will then recognise these proteins as foreign and produce its own protection (antibodies) against the viruses. If later on, the person comes into contact with SARS-CoV-2 or the influenza viruses, their immune system will recognise them and be ready to defend the body against them.

None of the ingredients in the vaccine can cause flu or COVID-19.

The vaccine targets three strains of influenza virus and one SARS-CoV-2 variant:

A/Wisconsin/67/2022 (A/H1N1)pdm09 .....8.3 micrograms RNA
A/Darwin/6/2021 (A/H3N2) .....8.3 micrograms RNA
B/Austria/1359417/2021 (B/Victoria lineage) .....8.3 micrograms RNA
SARS-CoV-2 Omicron XBB.1.5 .....6.7 micrograms RNA

The vaccine complies with the World Health Organisation (WHO) recommendations (Northern Hemisphere) and EU recommendations for the 2023/2024 season.

## 2. What you need to know before you are given mCOMBRIAX

**The vaccine must not be given if** you are **allergic** to the active substances 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 mCOMBRIAX if:

- you have previously had a severe, life-threatening allergic reaction after any other vaccine injection or after you were given mCOMBRIAX in the past.
- you have a very weak or compromised immune system.
- you have a bleeding disorder.
- you have a high fever or severe infection. In this case, the vaccination will be postponed. There is no need to delay vaccination for a minor infection, such as a cold, but talk to your doctor first.
- you have anxiety related to injections.

Cases of myocarditis and pericarditis (inflammation of the heart muscle or the membrane around the heart) have been reported for some other COVID-19 vaccines.

These conditions can develop within a few days and primarily occurred within 14 days. They have been observed 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 mCOMBRIAX.

As with all vaccines, mCOMBRIAX may not fully protect all people who are vaccinated.

**Children and adolescents**
mCOMBRIAX should not be used in children and adolescents. It has not been studied in this age group.

**Other medicines and mCOMBRIAX**
Tell your doctor, pharmacist or nurse if you are taking, have recently taken, or might take any other medicines.

**Immunocompromised individuals**
mCOMBRIAX may not work as well in people who are immunocompromised. If your immune system is weakened because of disease or medical treatment, you should continue to maintain physical precautions to help prevent flu and 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 breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before you are given this vaccine. No or limited data are available regarding the use of mCOMBRIAX during pregnancy and breast-feeding. mCOMBRIAX can be used during breast-feeding.

**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.

Some of the side effects of vaccination in section 4 (Possible side effects), like feeling tired, may temporarily affect the ability to drive or use machines. If you experience such side effect, wait until they have worn off before you drive or use machines.

## 3. How mCOMBRIAX is given

The recommended dose is one dose of 0.32 mL, given at least 3 months after the last dose of a COVID-19 vaccine.

mCOMBRIAX is given as a single injection in the muscle of the upper arm (deltoid muscle).

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 medicine can cause side effects, although not everybody gets them.

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

**Very common** (may affect more than 1 in 10 people)
- swelling/tenderness in the underarm (lymphadenopathy)
- headache
- feeling sick (nausea)
- vomiting
- muscle ache (myalgia)
- joint ache (arthralgia)
- pain at the injection site
- feeling tired (fatigue)
- chills
- fever (pyrexia)

**Common** (may affect up to 1 in 10 people)
- swelling at the injection site
- redness (erythema) at the injection site

**Uncommon** (may affect up to 1 in 100 people)
- diarrhoea
- itchiness at the injection site

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

**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 mCOMBRIAX

Your doctor, pharmacist or nurse is responsible for storing this vaccine and disposing of any unused product correctly. The following information is intended for healthcare professionals.

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 carton and syringe label after EXP. The expiry date refers to the last day of that month.

*Frozen vaccine*
Store in a freezer between -40 °C to -15 °C for up to 1 year.
Keep the pre-filled syringes in the outer carton in order to protect from light.

*Thawed vaccine*
Within the shelf life of 1 year, the vaccine is stable for 30 days when stored at 2 °C to 8 °C and protected from light. At the end of 30 days, the vaccine should be used immediately or discarded.

Once thawed, the vaccine should not be refrozen.

Upon moving the vaccine to 2 °C to 8 °C storage, the outer carton should be marked with the new expiry date at 2 °C to 8 °C.

The pre-filled syringes may be stored at 8 °C to 25 °C for up to 24 hours after removal from the refrigerated conditions. Within this period of time, pre-filled syringes may be handled in ambient light conditions. Do not refrigerate after being stored at 8 °C to 25 °C. Discard the syringe if not used within this time.

*Transportation of thawed pre-filled syringes*
Thawed pre-filled syringes can be transported at 2 °C to 8 °C using shipping containers which have been qualified to maintain 2 °C to 8 °C. Once thawed and transported 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.

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 mCOMBRIAX contains

The active substances are a combination of influenza virus of the following strains and SARS-CoV-2 mRNA.

| **Influenza virus strains and SARS-CoV-2** | **Per 0.32 mL dose** |
|---|---|
| A/H1N1 | 8.3 micrograms RNA |
| A/H3N2 | 8.3 micrograms RNA |
| B/Victoria lineage | 8.3 micrograms RNA |
| SARS-CoV-2 Omicron XBB.1.5 | 6.7 micrograms RNA |

mCOMBRIAX is a lipid nanoparticle-encapsulated, mRNA-based vaccine encoding antigens from seasonal influenza viruses and from SARS-CoV-2.

The other ingredients are: heptadecan-9-yl 8-{(2-hydroxyethyl)[6-oxo-6-(undecyloxy)hexyl]amino}octanoate (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, sucrose, water for injections.

### What mCOMBRIAX looks like and contents of the pack

mCOMBRIAX is a white to off-white dispersion for injection (pH: 7.1 – 7.8) provided in a pre-filled syringe.

mCOMBRIAX is available in packs containing 1 or 10 pre-filled syringes.

Not all pack sizes may be marketed.

Needles are not provided in the pack.

**Marketing Authorisation Holder and Manufacturer**
MODERNA BIOTECH SPAIN, S.L.
C/ Julián Camarillo nº 31
28037 Madrid
Spain

For any information about this vaccine, please contact the local representative of the Marketing Authorisation Holder:

**België/Belgique/Belgien**
Tél/Tel: 0800 81 460

**България**
Тел.: 0800 115 4477

**Česká republika**
Tel: 800 050 719

**Danmark**
Tlf.: 80 81 06 53

**Deutschland**
Tel: 0800 100 9632

**Eesti**
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Τηλ: +30 800 000 0030

**España**
Tel: 900 031 015

**France**
Tél: 0805 54 30 16

**Hrvatska**
Tel: 08009614

**Ireland**
Tel: 1800 800 354

**Ísland**
Sími: 800 4382

**Italia**
Tel: 800 928 007

**Κύπρος**
Τηλ: 80091080

**Latvija**
Tel: 80 005 898

**Lietuva**
Tel: 88 003 1114

**Luxembourg/Luxemburg**
Tél/Tel: 800 85 499

**Magyarország**
Tel.: 06 80 987 488

**Malta**
Tel: 8006 5066

**Nederland**
Tel: 0800 409 0001

**Norge**
Tlf: 800 31 401

**Österreich**
Tel: 0800 909636

**Polska**
Tel.: 800 702 406

**Portugal**
Tel: 800 210 256

**România**
Tel: 0800 400 625

**Slovenija**
Tel: 080 083082

**Slovenská republika**
Tel: 0800 191 647

**Suomi/Finland**
Puh/Tel: 0800 774198

**Sverige**
Tel: 020 10 92 13

**This leaflet was last revised in** .

**Other sources of information**

Detailed information on this vaccine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

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**The following information is intended for healthcare professionals only:**

Handling instructions for mCOMBRIAX before use

The vaccine is ready to use once thawed.

Do not dilute the product.

Do not shake the pre-filled syringe before use.

The pre-filled syringe is for single use only.

Do not use if the pre-filled syringe has been dropped or damaged or the security seal on the carton has been broken.

One (1) dose of 0.32 mL can be administered from each pre-filled syringe.

mCOMBRIAX is supplied in a single-dose, pre-filled syringe (without needle) containing 0.32 mL (31.7 micrograms of total RNA) and must be thawed prior to administration.

mCOMBRIAX is shipped and supplied either as a frozen or thawed pre-filled syringe (see section 5). If the vaccine is frozen, it must be completely thawed before use. Thaw each pre-filled syringe before use, either in the refrigerator or at room temperature, following the instructions in Table 1.

If the vaccine has been thawed at room temperature (15 °C to 25 °C), the pre-filled syringe is ready to administer. Syringes should not be returned to the refrigerator after being thawed at room temperature.

The pre-filled syringes may be stored at 8 °C to 25 °C for a total of 24 hours after removal from refrigerated conditions. Within this period of time, pre-filled syringes may be handled in ambient light conditions. Discard the syringe if not used within this time.

Thaw each pre-filled syringe before use following the instructions below. Pre-filled syringes may be thawed outside the carton or in the carton itself, either in the refrigerator or at room temperature (Table 1).

**Table 1. Thawing instructions for pre-filled syringes and cartons before use**

| **Configuration** | **Thaw instructions and durations** | | | |
|---|---|---|---|---|
| | **Thaw temperature (in a refrigerator) (°C)** | **Thaw duration (minutes)** | **Thaw temperature (at room temperature) (°C)** | **Thaw duration (minutes)** |
| One pre-filled syringe or a carton of 1 pre-filled syringe | 2 – 8 | 100 | 15 – 25 | 40 |

| Configuration | Thaw instructions and durations | | | |
|---|---|---|---|---|
| | **Thaw temperature (in a refrigerator) (°C)** | **Thaw duration (minutes)** | **Thaw temperature (at room temperature) (°C)** | **Thaw duration (minutes)** |
| Carton of 10 pre-filled syringes | 2 – 8 | 160 | 15 – 25 | 80 |

Administration

- After thawing, the vaccine cannot be re-frozen.
- The pre-filled syringe should be inspected visually for particulate matter and discolouration prior to administration.
- Do not administer if vaccine is discoloured 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).
- With tip cap upright, remove tip cap by twisting counter-clockwise until tip cap releases. Remove tip cap in a slow, steady motion. Avoid pulling tip cap while twisting.
- Attach the needle by twisting in a clockwise direction until the needle fits securely on the pre-filled syringe.
- Uncap the needle when ready for administration.
- The vaccine should be administered immediately after uncapping.
- Administer the entire dose intramuscularly.
- Discard the pre-filled syringe after single use.

Disposal

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