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Decision

Information for Healthcare Professionals on COVID-19 Vaccine Moderna

Updated 28 January 2021

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Regulation 174 Information for UK healthcare professionals

This medicinal product has been given authorisation for temporary supply by the UK Department of Health and Social Care and the Medicines and Healthcare products Regulatory Agency. It does not have a marketing authorisation, but this temporary authorisation grants permission for the medicine to be used for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus in individuals 18 years of age and older.

As with any new medicine in the UK, this product will be closely monitored to 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

COVID-19 Vaccine Moderna dispersion for injection

COVID-19 mRNA Vaccine (nucleoside modified)

2. Qualitative and quantitative composition

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

One dose (0.5 mL) contains 0.10 mg of mRNA (embedded in lipid nanoparticles).

COVID-19 mRNA vaccine is single-stranded, 5’-capped messenger RNA (mRNA) produced using cell-free in vitro transcription, encoding the pre-fusion stabilized Spike (S) glycoprotein of SARS-CoV-2.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Dispersion for injection

White to off-white frozen dispersion (pH: 7.0 – 8.0).

4. Clinical particulars

4.1 Therapeutic indications

COVID-19 Vaccine Moderna is indicated for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus in individuals 18 years of age and older.

The use of COVID-19 Vaccine Moderna should be in accordance with official guidance.

4.2 Posology and method of administration

COVID-19 Vaccine Moderna should be administered by a trained healthcare worker.

COVID-19 Vaccine Moderna vials are for multiple use. Each multidose vial contains 10 doses of 0.5 mL.

Posology

Individuals 18 years of age and older:

COVID-19 Vaccine Moderna is a two-dose regimen. Each dose is 0.5 mL. It is recommended to administer the second dose 28 days after the first dose (see section 5.1).

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

Paediatric population

The safety and efficacy of COVID-19 Vaccine Moderna in children and adolescents less than 18 years of age have not yet been established. No data are available.

Method of administration

COVID-19 Vaccine Moderna should only be administered by the intramuscular route. The preferred site is the deltoid muscle of the upper arm.

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

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

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

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Anaphylactic reactions

Events of anaphylaxis have been reported. Appropriate medical treatment and supervision to manage immediate allergic reactions must always be readily available in case of an acute anaphylactic reaction following administration of the COVID-19 Vaccine Moderna.

Close observation for at least 15 minutes is recommended following vaccination.

A second dose of COVID-19 Vaccine Moderna should not be given to those who have experienced severe allergic reactions (e.g. anaphylaxis, generalised urticaria) to the first dose of COVID-19 Vaccine Moderna (see section 4.3).

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.

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.

Immunocompromised individuals

Efficacy, safety and immunogenicity have not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of COVID-19 Vaccine Moderna may be less in these individuals.

Coagulation disorders

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

Acute illness

Immunization should be postponed in individuals with severe febrile illness or severe acute infection. Individuals with moderate or severe acute illness should be vaccinated as soon as the acute illness has improved.

Limitations of vaccine effectiveness

Vaccination with COVID-19 Vaccine Moderna may not protect all vaccine recipients. Individuals may not be fully protected until 14 days after their second dose. The duration of protection afforded by the vaccine is unknown at present. Reference should be made to section 5.1.

Excipients with known effect

Sodium

This vaccine contains less than 1 mmol sodium (23 mg) per 0.5 mL dose and is essentially ‘sodium-free’

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

There are no data to assess the concomitant administration of COVID-19 Vaccine Moderna with other vaccines (see section 5.1).

4.6 Fertility, pregnancy and lactation

Pregnancy

There is limited experience with use of COVID-19 Vaccine Moderna in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development (see section 5.3). Administration of COVID-19 Vaccine Moderna in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and foetus.

Breast-feeding

It is unknown whether COVID-19 Vaccine Moderna is excreted in human milk.

Fertility

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

4.7 Effects on ability to drive and use machines

No studies on the effects of the COVID-19 Vaccine Moderna on the ability to drive and use machines have been performed.

Some of the effects mentioned under section 4.8 “Undesirable Effects” may affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

The safety of COVID-19 Vaccine Moderna was evaluated in an ongoing Phase 3 randomized, placebo-controlled, observer-blind clinical trial conducted in the United States involving 30,351 participants 18 years of age and older who received at least one dose of COVID-19 Vaccine Moderna (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 injection site pain (92%), fatigue (70%), headache (65%), myalgia (62%), arthralgia (46%) chills (46%), 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 the second dose than after the first dose. If required, symptomatic treatment with analgesic and/or anti-pyretic medicinal products (e.g. paracetamol-containing products) may be used.

Tabulated list of adverse reactions

The safety profile presented below is based on data generated in a placebo- controlled clinical study of 30,351 adults ≥ 18 years of age.

Adverse reactions reported are listed according to the following frequency:

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)

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Adverse drug reactions (ADRs)

System Organ Class: Blood and lymphatic system disorders

Frequency: Very common

Adverse reactions: Lymphadenopathy

Lymphadenopathy was captured as axillary swelling/tenderness on the same side as the injection site.

System Organ Class: Immune system disorders

Frequency: Not known (cannot be estimated from the available data)

Adverse reactions: Anaphylaxis

Anaphylaxis has been reported in post-marketing setting

System Organ Class: Immune system disorders

Frequency: Not known (cannot be estimated from the available data)

Adverse reactions: Hypersensitivity

System Organ Class: Nervous system disorders

Frequency: Very common

Adverse reactions: Headache

System Organ Class: Nervous system disorders

Frequency: Rare

Adverse reactions: Facial paralysis

Throughout the safety follow-up period, acute peripheral facial paralysis (or palsy) was reported by three participants in the COVID-19 mRNA Vaccine 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.

System Organ Class: Gastrointestinal disorders

Frequency: Very common

Adverse reactions: Nausea, Vomiting

System Organ Class: Subcutaneous and skin disorders

Frequency: Common

Adverse reactions: Rash

System Organ Class: Musculoskeletal and connective tissue disorders

Frequency: Very common

Adverse reactions: Myalgia, Arthralgia

System Organ Class: General disorders and administration site conditions

Frequency: Very common Adverse reactions: Injection site pain , fatigue, chills, pyrexia, injection site swelling

System Organ Class: General disorders and administration site conditions

Frequency: Common

Adverse reactions: injection site erythema, injection site urticaria, injection site rash

System Organ Class: General disorders and administration site conditions

Frequency: Uncommon Adverse reactions: Injection site pruritus

System Organ Class: General disorders and administration site conditions

Frequency: Rare Adverse reactions: Swelling face

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 1 and 2 days, respectively, after vaccination and was likely related to vaccination.

The reactogenicity and safety profile in 343 subjects receiving COVID-19 Vaccine Moderna, that were seropositive for SARS-CoV-2 at baseline, was comparable to that in subjects seronegative for SARS-CoV-2 at baseline.

Reporting of suspected adverse reactions

If you are concerned about an adverse event, it should be reported on a Yellow Card. Reporting forms and information can be found at Coronavirus Yellow Card reporting site (https://coronavirus-yellowcard.mhra.gov.uk/) or search for MHRA Yellow Card in the Google Play Store (https://play.google.com/store/apps/details?id=uk.org.mhra.yellowcard) and include the vaccine brand and batch/Lot number if available.

Alternatively, adverse events of concern in association with COVID-19 Vaccine Moderna can be reported to Moderna on the toll-free number: 08000857562, via Moderna COVID19 Global.

Please do not report the same adverse event(s) to both systems as all reports will be shared between Moderna and MHRA (in an anonymised form) and dual reporting will create unnecessary duplicates.

4.9 Overdose

No case of overdose has been reported.

In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

5. Pharmacodynamic properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vaccine, covid-19 vaccines, ATC code: J07BX03

Mechanism of action

COVID-19 Vaccine Moderna encodes for the pre-fusion stabilized Spike protein of SARS-CoV-2. After intramuscular injection, cells at the injection site take up the lipid nanoparticle, effectively delivering the mRNA sequence into cells for translation into protein. The mRNA delivery system is based on the principle and observation that cells in vivo can take up mRNA, translate it, and express viral protein antigen(s) in the desired conformation. The delivered mRNA does not enter the cellular nucleus or interact with the genome, is nonreplicating, and is expressed transiently. The protein undergoes post-translational modification and trafficking resulting in properly folded, fully functional Spike protein that is inserted into the cellular membrane of the expressing cell(s). The Spike protein is membrane bound, mimicking the presentation of natural infection.

The expressed Spike protein of SARS-CoV-2 is then recognized by immune cells as a foreign antigen which elicits both T-cell and B-cell responses. The immune response to the Spike protein results in functional antibody and T-cell responses and in the generation of memory immune cell populations.

The specific mechanism of protection for the SARS-CoV-2 virus remains under investigation.

Clinical efficacy

A randomized, placebo-controlled, observer-blind clinical study was conducted in subjects 18 years of age and older who were at increased risk of COVID-19 disease. In addition, pre-specified cohorts of subjects who were either ≥65 years of age or 18 to < 65 years of age with comorbid medical conditions were included. The study excluded individuals who were immunocompromised or had received immunosuppressants within 6 months. Participants with stable HIV disease were not excluded. Individuals with a known history of SARS-CoV-2 infection were also excluded. Influenza vaccines could be administered 14 days before or 14 days after any dose of COVID-19 Vaccine Moderna. 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 COVID-19 Vaccine Moderna.

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

The primary efficacy analysis population (referred to as the Per Protocol Set or PPS), included 28,207 subjects who received either Moderna COVID-19 vaccine (n=14,134) or placebo (n=14,073), had a negative baseline SARS-CoV-2 status, and did not develop confirmed COVID-19 within 14 days after the second dose. The PPS study population included 47.4% female, 52.6% male, 19.7% Hispanic or Latino, and 9.7% African American. The median age of subjects was 53 years (range 18-94). A dosing window of –7 to +14 days was allowed for inclusion in the PPS. The proportion of vaccinees who received the second dose per protocol (-3 to +7) (25d to 35 days after dose 1) was 98%.

COVID-19 cases were confirmed by Polymerase Chain Reaction (PCR) and by a Clinical Adjudication Committee.

Table: Primary Efficacy Analysis: confirmed COVID-19# regardless of severity starting 14 days after the 2nd dose – Per-Protocol Set

Age Group (Years)	Moderna COVID-19 Vaccine	Moderna COVID-19 Vaccine	Moderna COVID-19 Vaccine	Placebo	Placebo	Placebo	% Vaccine Efficacy (95% CI)*	

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

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

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

Efficacy against severe COVID-19

Among all subjects in the PPS, no cases of severe COVID-19 were reported in the vaccine group compared with 30 cases reported in the placebo group (incidence rate 9.138 per 1,000 persons/years). Vaccine efficacy against severe COVID-19 was 100% (87.0, 100).

Table: Secondary Efficacy Analysis: confirmed severe COVID-19# cases starting 14 days after the 2nd dose – -Per-protocol Set

Endpoint	Moderna COVID-19 Vaccine	Moderna COVID-19 Vaccine	Moderna COVID-19 Vaccine	Placebo	Placebo	Placebo	% Vaccine Efficacy (95% CI)*
-	Subjects N	COVID-19 Cases n	Incidence Rate of COVID-19 per 1,000 Person-Years	Subjects N	COVID-19 Cases n	Incidence Rate of COVID-19 per 1,000 Person-Years	-
Severe* cases 14 days after dose 2	14,134	0	NA	14,073	30	9.138	100% (87.0, 100)

Severe COVID-19 cases are defined as a confirmed COVID-19 as per the Primary Efficacy Endpoint case definition, plus any of the following:

- Clinical signs indicative of severe systemic illness, Respiratory Rate ≥ 30 per minute, Heart Rate ≥ 125 beats per minute, SpO2 ≤ 93% on room air at sea level or PaO2/FIO2 < 300 mm Hg, OR
- Respiratory failure or Acute Respiratory Distress Syndrome (ARDS), (defined as needing high-flow oxygen, non-invasive or mechanical ventilation, or ECMO), evidence of shock (systolic blood pressure < 90 mmHg, diastolic BP < 60 mmHg or requiring vasopressors),

OR

- Significant acute renal, hepatic or neurologic dysfunction, OR
- Admission to an intensive care unit or death.
- VE and 95% CI from the stratified Cox proportional hazard model

Additional Efficacy Analyses

Table 4: Subgroup Analyses of Vaccine Efficacy - COVID-19 14 days after dose 2 per Adjudication Committee Assessments (primary efficacy analysis set) – Per-protocol Set

Subgroup	Moderna COVID-19 Vaccine	Moderna COVID-19 Vaccine	Moderna COVID-19 Vaccine	Placebo	Placebo	Placebo	% Vaccine Efficacy (95% CI)*

-	Subjects N	COVID-19 Cases n	Incidence Rate of COVID-19 per 1,000 Person-Years	Subjects N	COVID-19 Cases n	Incidence Rate of COVID-19 per 1,000 Person-Years	-
Overall High risk*	3,206	4	5.227	3,167	43	57.202	90.9 (74.7, 96.7)
High risk 18 to <65	2,155	2	3.947	2,118	35	70.716	94.4 (76.9, 98.7)
Not High risk 18 to <65	8,396	5	2.594	8,403	121	63.054	95.9 (90.0,98.3)
Females	6,768	7	4.364	6,611	98	62.870	93.1 (85.2,96.8)
Males	7,366	4	2.352	7,462	87	50.730	95.4 (87.4,98.3)
White***	9,023	10	4.413	8,916	144	64.608	93.2 (87.1, 96.4)
Communities of color***	5,088	1	-	5,132	41	-	97.5 (82.2, 99.7)

First *: Subjects at increased risk of severe COVID-19 due to at least one pre-existing medical condition (chronic lung disease, significant cardiac disease, severe obesity, diabetes, liver disease or HIV infection), regardless of age

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

***White is defined as non-Hispanic white, and communities of colour is defined as all others except those whose race and ethnicity were both reported as unknown, not reported, or were both missing.

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

Elderly population

COVID-19 Vaccine Moderna was assessed in individuals 18 years of age and older, including 3,768 subjects 65 years of age and older. The efficacy of COVID-19 Vaccine Moderna was consistent between older subjects (≥65 years) and younger subjects (18-64 years). Older subjects 65 years of age and over reported solicited local and systemic adverse reactions at a lower rate than younger subjects 18-64 years of age (see section 4.8).

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

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

6. Pharmaceutical particulars

6.1 List of excipients

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

The list of excipients is:

- Lipid SM-102
- Cholesterol
- 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC)
- 1,2-Dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG2000-DMG)
- Trometamol (Tris)
- Trometamol hydrochloride (Tris HCl)
- 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

7 months at -25ºC to -15ºC.

After thawing

Once thawed, the medicinal product should not be re-frozen and may be stored refrigerated at 2 °C to 8 °C protected from light for up to 30 days if not used (needle-punctured).

Chemical and physical stability of an unopened vial after removal from refrigerated conditions has been demonstrated for 12 hours at 8° to 25°C. Do not refreeze.

Punctured Vial:

Chemical and physical in-use stability has been demonstrated for 6 hours at 2 to 25 ºC after first puncture. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

COVID-19 Vaccine Moderna multiple-dose vials are stored frozen between -25º to -15ºC. Do not store or transport on dry ice or below -40ºC. Once thawed, do not re-freeze.

Protect from light.

For storage conditions after thawing of the medicinal product, see section 6.3.

6.5 Nature and contents of container

COVID-19 Vaccine Moderna is supplied in a type 1 or type 1 equivalent glass vial with stopper (chlorobutyl rubber) and seal (aluminium, flip-off) containing 5 mL dispersion.

Vials are packaged in a carton containing a total of ten multidose vials per carton. Each vial contains 10 doses of 0.5 mL each.

Pack size: 10 vials

6.6 Special precautions for disposal and other handling

COVID-19 Vaccine Moderna vials are for multiple use. Each multidose vial contains 10 doses of 0.5 mL.

COVID-19 Vaccine Moderna multidose vials are stored frozen between -25 °C to -15 °C until ready for use. Do not store on dry ice or below -40 ºC.

Remove the required number of vials from freezer storage and thaw each vial before use:

- thaw in refrigerated conditions between 2 °C to 8 °C for 2 ½ hours. Let each vial stand at room temperature for 15 minutes before administering.
- alternatively, thaw at room temperature between 15 °C to 25 °C for 1 hour.
- do not re-freeze vials after thawing.

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

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

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

This product is preservative-free. Once the vial has been used (needle-punctured) to withdraw the initial dose, the vaccine should be used immediately. Any unused vaccine should be discarded after 6 hours.

If not used immediately, in-use storage times and conditions are the responsibility of the user.

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

7. Marketing authorisation holder

Not applicable.

8. Marketing authorisation number(s)

Not applicable.

9. Date of first authorisation/renewal of the authorisation

Not applicable.

10. Date of revision of the text

26 January 2021

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