UK Medical Freedom ALLIANCE

Novavax COVID-19 Vaccine
PATIENT INFORMATION LEAFLET

This leaflet should be used alongside the UKMFA general COVID-19 Vaccines Patient Information Leaflet[i]. It contains general medical information which is not advice and should not be treated as such.

SUMMARY

- In January 2020, Novavax announced development of vaccine candidate NVX-CoV2373 to establish immunity to SARS-CoV-2
- The MHRA granted conditional authorisation for **Novavax** NVX-CoV2373 on 3 February 2022 for the UK[ii]
- NVX-CoV2373 is sold under the name of Nuvaxovid or Covovax and has "conditional", not full, marketing authorisation[iii]
- Novavax is required to provide additional information on vaccine stability (31 July 2023). The product life cycle and assessment of the finished product potency limits must also be reviewed when additional data becomes available (31 July 2022)[iv]
- Product Phase 3 clinical trials are ongoing - set to complete 30 June 2023 (final data collection date for primary outcome measure)[v]
- The MHRA based authorisation on two trials – PREVENT-19 which enrolled approximately 30,000 people in the US and Mexico, and a separate trial of around 15,000 participants in the UK. Results of both trials were published in the New England Journal of Medicine[vi]

VACCINE TYPE AND DOSE

Vaccine type

- Nuvaxovid is marketed as a more "traditional vaccine" using familiar technology already used in a few approved products
- It is a **protein subunit vaccine**, however unlike other subunit preparations it **contains spike proteins** derived and manufactured from moth cells
- The **Matrix-M adjuvant** uses **saponin** extracted from the Chilean soapbark tree (*Quillaja saponaria*)

How it works

- Nuvaxovid is produced for **intramuscular injection**
- Novavax's **NVX-CoV2373** is engineered from the genetic sequence of SARS-CoV-2 and uses recombinant nanoparticle technology to generate an antigen derived from the coronavirus spike (S) protein. The SARS-CoV-2 rS Protein active substance is produced in an Sf9 insect cell line by using a recombinant baculovirus system[vii]
- It is co-formulated using **Novavax's patented saponin-based Matrix-M™ adjuvant** to enhance the immune response and stimulate high levels of neutralising antibodies[viii]
- *"Novavax's candidate differs from those currently being used in the UK, combining an engineered protein from the virus that causes COVID-19 with a plant-based ingredient to help generate a stronger immune response"*[ix]

Doses required

- Two 0.5 ml doses (5µg antigen and 50µg Matrix-M adjuvant) given intramuscularly 21 days apart, in adults ≥ 18 years of age[x]

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INGREDIENTS

- Nuvavaxoid contains **spike protein** and uses **Lipid Nanoparticle (LNP)** technology. Nuvaxovid does not contain PEG[xi]
- Claim that **no raw materials of animal or human origin used** during the manufacturing process of the active substance
- Three materials of biological origin used in the active substance process, namely **Insect Cell Media** (yeast), **Nutrient feed** (soy), and **Affinity Resin**[xii]
- One dose (0.5 mL) of Nuvaxovid contains **5µg of SARS-CoV-2 spike protein** and is **adjuvanted with Matrix-M**.
- The **spike protein** is produced by **recombinant DNA technology** using a baculovirus expression system in an insect cell line that is derived from Sf9 cells of the Spodoptera frugiperda species
- **Matrix-M** is a new adjuvant (meant to accelerate, improve, and/or prolong the protective effects of the vaccine) made from **saponin**, a compound for which toxicity, haemolytic and stability concerns have been raised by researchers[xiii] [xiv]
- Matrix-M adjuvant contains **Fraction-A** (42.5µg) and **Fraction-C** (7.5µg) of **enriched purified bark extract** (Quillaia Saponaria Molina) extract per 0.5 mL dose as well as **cholesterol** of botanical origin, and **phosphatidylcholine** from hen's egg yolk[xv]
- Novavax initiated trials with and without Matrix-M (due to complete 21 May 2022)[xvi] *"Novavax's patented saponin-based Matrix-M™ adjuvant has demonstrated a potent and well-tolerated effect by stimulating the entry of antigen-presenting cells into the injection site and enhancing antigen presentation in local lymph nodes, boosting immune response"*[xvii] [xviii]

Other ingredients (excipients) in Nuvaxovid are:

- Disodium hydrogen phosphate heptahydrate
- Sodium dihydrogen phosphate monohydrate
- Disodium hydrogen phosphate dihydrate
- Sodium chloride
- Polysorbate 80
- Potassium dihydrogen phosphate (buffer)
- Potassium chloride (tonicity agent)
- Sodium hydroxide (for the adjustment of pH)
- Hydrochloric acid (for the adjustment of pH)
- Water for injections[xix]

ANIMAL TRIALS

Non-clinical toxicology studies - NVX-CoV2373 was shown to induce both cellular and humoral immune responses across multiple species, including rodents and non-human primates.

- **Mice** - low-dose NVX-CoV2373 with Matrix-M elicited high titre anti-S IgG blocking hACE2 receptor binding, neutralising virus, and protecting against SARS-CoV-2 challenge. Evidence was said not to show vaccine-associated enhanced respiratory disease (VAERD)
- **Baboons** - low-dose NVX-CoV2373 with Matrix-M was highly immunogenic and elicited high titre anti-S antibodies and functional antibodies, blocking S-protein binding to hACE2 and neutralizing virus infection and antigen-specific T cells[xx]
- As Novavax vaccine is intended for use in adults > 18 years, manufacturers stated **"no juvenile animal studies are needed"**[xxi]

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HUMAN TRIALS

Phase 1, 2 and 3 trials remain active - Novavax must provide the interim and final study reports to the MHRA as soon as they become available.

Phase 1/2 18-59 years

- Randomised, observer-blinded, placebo-controlled trial of NVX-CoV2373 started May 2020[xxii]
- 131 healthy men and nonpregnant women volunteers aged 18-59 at two Australian sites.
- Evaluated two doses (administered 21 days apart) of NVX-CoV2373 across two dose levels (5 µg and 25 µg), with and without the Matrix-M™ adjuvant
- 83 participants received the vaccine with adjuvant, 25 received vaccine without adjuvant, and 23 participants received placebo (sterile 0.9% normal saline)

Phase 2 Trials

- Commenced August 2020 - designed to identify the dosing regimen of NVX-CoV2373. Trial assessed two dose strengths (5 and 25 µg), each with 50 µg of Matrix-M[xxiii]
- Conducted at 9 sites in Australia and 8 sites in the US
- 1,622 healthy men and non-pregnant women aged 18-84 years, with a body mass index of 17-35. Around 50% of participants ≥60 years of age
- Participants with underlying medical conditions included if their conditions were clinically stable. Participants with confirmed COVID-19 presenting with mild symptomatology were also included

Phase 3 Trials

- **September-November 2020 – Randomised, observer-blinded, placebo-controlled trial conducted at 33 sites in the United Kingdom** to evaluate the efficacy, safety and immunogenicity of NVX-CoV2373 with Matrix-M[xxiv]
- **14,039 trial participants**, including participants who had stable chronic medical conditions. 44.6% had coexisting illnesses
- **Key exclusion criteria - a history of documented COVID-19, treatment with immunosuppressive therapy, or a diagnosis of an immunodeficient condition**
- Participants received 2 intramuscular 5-µg doses of NVX-CoV2373 or placebo, administered 21 days apart. Half of participants received 2 intramuscular injections of vaccine (5 µg of protein antigen with 50 µg Matrix-M adjuvant) administered 21 days apart, and half the trial participants received placebo (saline)
- **Another Phase 3, randomised, observer-blinded, placebo-controlled trial** commenced in the **US and Mexico in first half of 2021**[xxv] Evaluated efficacy and safety of NVX-CoV2373 in adults (≥18 years of age) who had not had SARS-CoV-2 infection.
- Participants randomly assigned in 2:1 ratio to receive two doses of NVX-CoV2373 or placebo 21 days apart
- Of the **29,949 participants**, a total of 29,582 (median age 47 years; 12.6% ≥65 years of age) received at least one dose: 19,714 received vaccine and 9,868 placebo
- **Exploratory Phase 3 (2019nCoV-302) sub-study**[xxvi], licensed, inactivated **seasonal influenza vaccines were co-administered to participants** on the same day as Dose 1 of Nuvaxovid (n = 217) or placebo (n = 214) in the opposite deltoid muscle of the arm in 431 participants

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SIDE EFFECTS

Phase 1 Trial Side-Effects

- 1st Dose – Novavax reported Phase 1 data in early August 2020[xxvii], stating that **the vaccine was generally well-tolerated and elicited robust antibody responses**

  The most commonly reported **local reactions (80%) were pain and tenderness**, and the most common **systemic reactions (>60%) were headache, fatigue and myalgia**. Most reactions were mild or moderate. **Two participants (2%) had severe adverse events (headache, fatigue, and malaise**). Laboratory abnormalities of grade 2 or higher occurred in 13 participants (10%)

- 2nd Dose – **Reactogenicity was greater following the second dose**. At the time of writing the supplementary information was not available[xxviii]

Phase 2 Trial Side-Effects

- Local adverse events were higher in the NVX-CoV2373 groups than in the placebo group following each vaccination
- Most frequent local adverse events across both age groups were **tenderness** (48% and 59%, respectively) and **pain** (27% and 38%). The frequencies of these events were **higher among younger participants** (61% and 68% for tenderness; 36% and 48% for pain) and lower among older participants (33% and 49% for tenderness; 17% and 25% for pain)
- **Grade 3 local adverse events** were reported in one low-dose (<1%) and two high-dose recipients (1%) among younger participants and in one high-dose recipient (<1%) among older participants; **there were no grade 4 events**.
- **Seven participants dropped out of the trial** due to an unsolicited adverse event, including two placebo recipients (non-Hodgkin's lymphoma; atrial fibrillation); one low-dose recipient (urinary incontinence); and four high-dose recipients (arthralgia; pyrexia, myalgia, and malaise (related); dermatitis; and atrial fibrillation.
- **Nine serious adverse events were reported**:
  - 1 case of **acute colitis** (assessed as related)
  - 1 case of **atrial fibrillation** (not related due to underlying cardiac disease)
  - 1 case of **vertigo** (not related)
  - 1 case of **wrist fracture** (not related)
  - 1case of **non-Hodgkin's lymphoma** (not related)
  - 1 case of **animal bite** (not related)
  - 1 case of **acute myocardial infarction** (not related as pre-existing hypertension, diabetes, hypercholesterolemia)
  - 1 case of **multiple sclerosis** in placebo group (assessed as related
  - 1 case of **lumbar spinal stenosis** (not related)
- One placebo recipient had an adverse event of special interest (multiple sclerosis), and there were **no adverse events of special interest associated with COVID-19**[xxix]

Phase 3 Trial Side-Effects

- **2,310 participants** included in subgroup in which adverse events were solicited[xxx]
- **Local adverse events were reported more frequently in the vaccine group than in the placebo group** after both the first dose (57.6% vs. 17.9%) and the second dose (79.6% vs. 16.4%)

- In vaccine recipients, most common local adverse events were **injection-site tenderness or pain** after both the first dose (with 53.3% reporting tenderness and 29.3% reporting pain) and the second dose (76.4% and 51.2%, respectively). **Most events Grade 1 (mild) or 2 (moderate) in severity and short mean duration** (2.3 days of tenderness and 1.7 days of pain after first dose and 2.8 and 2.2 days, respectively, after second dose)
- Local adverse events were **reported more frequently among younger vaccine recipients** (18 to 64 years of age) than among older recipients (≥65 years)
- Throughout clinical trials, an **increased incidence of hypertension following vaccination with Nuvaxovid** (n=46, 1.0%) as compared to placebo (n=22, 0.6%) was observed in older adults during the 3 days following vaccination[xxxi]
- In **Study 301 (US/MX)**[xxxii], the overall frequency of deaths was low and balanced between study groups. A total of **11 (< 0.1%) participants in the NVX-CoV2373 group and 5 (< 0.1%) participants in the placebo group died** during the pre-crossover period. None of the deaths were assessed by either the investigator or sponsor as related to the trial vaccine
- Deaths from cardiac disorders in Study 301 were more frequent in the placebo group than NVX-CoV2373 group, both pre- and post-crossover. Cardiac arrest was the most frequent cause of death in both treatment groups during the pre-crossover period
- Slightly higher frequency of unsolicited AEs leading to the second dose being withheld in the NVX-CoV2373 group in Study 301 compared to placebo: 52 (0.3%) vs 23 (0.2%), respectively
- **Grade 4 systemic adverse events were reported in 3 vaccine recipients**
- A thorough safety analysis noted a **higher incidence of SAEs of cholecystitis or acute cholecystitis in vaccine recipients compared to placebo** - **overall frequency was low**
- **Novavax considers myocarditis/pericarditis to be an important potential risk** and will continue to closely monitor and evaluate the data on this risk as they accrued 2 events (0.007%) in NVX-CoV2373 and 1 event (0.005%) in placebo

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VACCINE EFFICACY

Phase 3 US/Mexico Trial

Trial of 29,960 adults **claimed**[xxxiii]

- **90.4% efficacy** in preventing symptomatic COVID-19
- **100% protection** against moderate and severe disease
- **91.0% efficacy** in preventing symptomatic COVID-19 disease in people at high risk of complications from COVID-19

Efficacy Claims

- Phase 3 UK Trial - Two-doses of the NVX-CoV2373 vaccine administered to adult participants conferred **89.7% protection** against SARS-CoV-2 infection and showed high efficacy against the B.1.1.7 variant[xxxiv]

- Novavax COVID-19 vaccine is **89.3% effective at preventing COVID-19** - interim analysis of its Phase 3 study data, including effectiveness against the new variants of concern[xxxv]

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VACCINE SAFETY

Safety concerns/potential risks recognised for Nuvaxovid:

- **Vaccine-associated enhanced disease (VAED**), including vaccine associated enhanced respiratory disease (VAERD)
- **Anaphylaxis**
- **Myocarditis and pericarditis**

Missing information[xxxvi] [xxxvii]

- Safety and efficacy of Nuvaxovid in children (<18 years) not yet established. No data are available
- No data on use in pregnancy or breastfeeding
- No data on use in immunocompromised patients
- No data on use in frail patients with comorbidities (e.g., chronic obstructive pulmonary disease (COPD), diabetes, chronic neurological disease, cardiovascular disorders
- No data on use in those with autoimmune or inflammatory disorders
- Interaction with other vaccines unknown
- Long-term safety not established

Side effects

Local: pain, tenderness, erythema, and swelling

Systemic: fever, nausea/vomiting, headache, fatigue, malaise, myalgia, and arthralgia

One case of neuropathy from Study 302 (UK) vaccine recipient met the Brighton Collaboration case definition for **Guillain-Barré syndrome**[xxxviii]

Pregnancy/Breastfeeding

- The use of NVX-CoV2373 vaccine in pregnancy and during breastfeeding has not been studied
- Pregnant or breastfeeding women were excluded from participation in all clinical studies with NVX- CoV2373
- For women of childbearing potential, a urine pregnancy test was performed initially and prior to each study vaccination. A positive pregnancy test resulted in participant not receiving the vaccine
- **As of 15 March 2022, a total of 147 pregnancies, 136 pregnancies, 25 miscarriages, 41 live births**, were reported across the entire period of the clinical studies in participants who received NVXCoV2373[xxxix]

COST/STORAGE

- UK government procured 60 million doses of the Novavax candidate, the bulk will be manufactured in the UK
- Cost - £38 per dose[xl]
- Vaccine stable at 2°C to 8°C
- Unopened Nuvaxovid vaccine stable up to 12 hours at 25°C[xli]

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PLEASE DO YOUR OWN RESEARCH AND SPEAK TO YOUR DOCTOR

For further information about COVID-19 vaccines go to:

- Nuvaxavoid full manufacturer's package insert (SmPC) for professionals (not the simplified Patient Leaflet) available here
- UKMFA have published a COVID-19 Vaccine Informed Consent Form to help support discussions between a patient and the administering health professional about the benefits and risks of a COVID-19 vaccine
- For more information about Medical Freedom, Informed Consent and COVID-19 vaccines, please visit our website

You must not rely on the information on our website as an alternative to medical advice from your doctor or other professional healthcare provider. If you have any specific questions about any medical matter, you should consult your doctor or other professional healthcare provider.

[i] https://uploads-ssl.webflow.com/5fa5866942937a4d73918723/6006c4e4ccf7a9074538c6ad_UKMFA_COVID-19_Vaccine_Patient_Information.pdf

[ii] https://www.gov.uk/government/news/novavax-covid-19-vaccine-nuvaxovid-approved-by-mhra

[iii] https://www.gov.uk/guidance/conditional-marketing-authorisations-exceptional-circumstances-marketing-authorisations-and-national-scientific-advice

[iv] https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-nuvaxovid/conditional-marketing-authorisation-conditions-for-nuvaxovid-dispersion-for-injection

[v] https://clinicaltrials.gov/ct2/show/NCT04611802

[vi] https://www.pmlive.com/pharma_news/mhra_issues_cma_for_novavax_covid-19_vaccine_1387276

[vii] https://www.ema.europa.eu/en/documents/assessment-report/nuvaxovid-epar-public-assessment-report_en.pdf

[viii] https://ir.novavax.com/2022-06-07-FDA-Advisory-Committee-Recommends-Emergency-Use-Authorization-of-Novavax-COVID-19-Vaccine-for-People-Aged-18-Years-and-Older?sf165830302=1

[ix] https://www.gov.uk/government/news/novavax-publishes-positive-efficacy-data-for-its-covid-19-vaccine

[x] https://ir.novavax.com/2022-06-07-FDA-Advisory-Committee-Recommends-Emergency-Use-Authorization-of-Novavax-COVID-19-Vaccine-for-People-Aged-18-Years-and-Older?sf165830302=1

[xi] https://www.nebraskamed.com/COVID/moths-and-tree-bark-how-the-novavax-vaccine-works

[xii] https://www.ema.europa.eu/en/documents/assessment-report/nuvaxovid-epar-public-assessment-report_en.pdf

[xiii] https://pubmed.ncbi.nlm.nih.gov/19208455/

[xiv] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7738204/

[xv] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1071576/Nuvaxovid_final_PAR_PLGB_54180_0002.pdf

[xvi] https://www.clinicaltrials.gov/ct2/show/NCT04368988

[xvii] https://www.polypeptide.com/news/polypeptide-group-selected-by-novavax-to-manufacture-critical-intermediates-of-matrix-m-adjuvant-for-its-covid-19-vaccine/

[xviii] https://ir.novavax.com/2021-06-14-Novavax-Announces-Positive-Results-from-First-Study-of-Influenza-Vaccine-and-COVID-19-Vaccine-Candidate-Administered-Simultaneously

[xix] https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-nuvaxovid/product-information-leaflet-pil-for-nuvaxovid-dispersion-for-injection

[xx] https://www.nature.com/articles/s41467-020-20653-8

[xxi] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1071576/Nuvaxovid_final_PAR_PLGB_54180_0002.pdf

[xxii] https://www.nejm.org/doi/full/10.1056/NEJMoa2026920

[xxiii] https://www.medrxiv.org/content/10.1101/2021.02.26.21252482v1.full

[xxiv] https://www.nejm.org/doi/full/10.1056/NEJMoa2107659

[xxv] https://www.nejm.org/doi/10.1056/NEJMoa2116185

[xxvi] https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-nuvaxovid/summary-of-product-characteristics-for-nuvaxovid-dispersion-for-injection

[xxvii] https://www.bloomberg.com/press-releases/2020-09-02/novavax-announces-publication-of-phase-1-data-for-covid-19-vaccine-candidate-in-the-new-england-journal-of-medicine

[xxviii] https://www.nejm.org/doi/suppl/10.1056/NEJMoa2026920/suppl_file/nejmoa2026920_appendix.pdf

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[xxx] https://www.nejm.org/doi/full/10.1056/NEJMoa2107659

[xxxi] https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-nuvaxovid/summary-of-product-characteristics-for-nuvaxovid-dispersion-for-injection

[xxxii] https://www.fda.gov/media/158914/download

[xxxiii] https://www.nih.gov/news-events/news-releases/us-clinical-trial-results-show-novavax-vaccine-safe-prevents-covid-19

[xxxiv] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8262625/

[xxxv] https://www.nihr.ac.uk/news/novavax-covid-19-vaccine-893-effective/26720

[xxxvi] https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-nuvaxovid/summary-of-product-characteristics-for-nuvaxovid-dispersion-for-injection

[xxxvii] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1071576/Nuvaxovid_final_PAR_PLGB_54180_0002.pdf

[xxxviii] https://www.fda.gov/media/158914/download

[xxxix] https://www.fda.gov/media/158914/download

[xl] https://adisinsight.springer.com/drugs/800057632

[xli] https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-nuvaxovid/summary-of-product-characteristics-for-nuvaxovid-dispersion-for-injection