

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

COVID-19 Vaccine Valneva suspension for injection.
COVID-19 vaccine (inactivated, adjuvanted, adsorbed).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

This is a multi-dose vial which contains 10 single doses of 0.5 mL (see section 6.5).

One dose (0.5 mL) contains no less than 25 Antigen Units (AU) of inactivated SARS-CoV-2.

Highly purified whole virus SARS-CoV-2 antigen¹, inactivated² and adjuvanted with CpG 1018³ in combination with aluminium hydroxide⁴.

¹ Produced on Vero cells

² Inactivated with beta-propiolactone

³ 1 mg CpG1018 (cytosine phospho-guanine) adjuvant/0.5 mL dose

⁴ Adsorbed on aluminium hydroxide (0.5 mg Al³⁺)/0.5 mL dose

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection (injection).

White to off-white suspension (pH 7.5 ± 0.5).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

COVID-19 Vaccine Valneva is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in adults from 18 to 50 years of age.

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

4.2 Posology and method of administration

Posology

Individuals from 18 to 50 years of age

COVID-19 Vaccine Valneva is administered intramuscularly as a course of 2 doses (0.5 mL each). It is recommended to administer the second dose at least 28 days after the first dose (see section 5.1).

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

Paediatric population

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

Elderly population

The safety and immunogenicity of COVID-19 Vaccine Valneva in individuals ≥ 65 years of age have not yet been established. Very limited data are currently available in subjects over 50 years of age. See also sections 4.8 and 5.1.

Method of administration

COVID-19 Vaccine Valneva should be administered intramuscularly in the deltoid muscle. 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 on the 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

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

Anxiety-related reactions

Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. It is important that precautions are in place to avoid injury from fainting.

Concurrent illness

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

Thrombocytopenia and coagulation disorders

As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration in these individuals.

Immunocompromised individuals

The efficacy, safety and immunogenicity of the vaccine has not been assessed in immunocompromised individuals, including those receiving immunosuppressant therapy. The efficacy of COVID-19 Vaccine Valneva may be lower in immunosuppressed individuals.

Limitations of vaccine effectiveness

Based on immunogenicity data, no protection is anticipated after the first vaccine dose and individuals may not be fully protected until 14 days after their second dose. As with all vaccines, vaccination with COVID-19 Vaccine Valneva may not protect all vaccine recipients (see section 5.1).

Excipients

This vaccine contains potassium, less than 1 mmol (39 mg) per 0.5 mL dose, i.e. essentially 'potassium-free'.

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

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

Concomitant administration of COVID-19 Vaccine Valneva with other vaccines has not been studied.

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Breast-feeding

It is unknown whether COVID-19 Vaccine 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

COVID-19 Vaccine Valneva 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

The safety of COVID-19 Vaccine Valneva was evaluated in an ongoing Phase III randomised study conducted in the United Kingdom in about 4,000 healthy adults (or with a stable medical condition) divided in two cohorts, about 1,000 < 30 years and 3,000 ≥ 30 years. In total, 3,037 participants received COVID-19 Vaccine Valneva and 995 received Vaxzevria. The median age of the participants was 33 years, with less than 1% above 50 years. The median duration of follow-up after the second dose was 126 days.

The most frequently reported adverse reactions were injection site tenderness (> 60%) and pain (> 40%), fatigue (> 50%), headache (> 30%), muscle pain (> 30%) and nausea/vomiting (> 10%). The majority of adverse reactions were mild and resolved within 2 days of vaccination. The incidence and severity of adverse reactions were similar after the first and second doses. They tended to decrease with age.

COVID-19 Vaccine Valneva appeared less reactogenic than Vaxzevria in participants aged 30 years and older.

Tabulated list of adverse reactions

Adverse reactions reported are listed per MedDRA system organ class and according to the following frequency categories: Very common ($\geq 1/10$); Common ($\geq 1/100$ to $< 1/10$); Uncommon ($\geq 1/1,000$ to $< 1/100$); Rare ($\geq 1/10,000$ to $< 1/1,000$); Very rare ($< 1/10,000$); Not known (cannot be estimated from available data)

MedDRA System Organ Class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Uncommon	Lymphadenopathy
Nervous System Disorders	Very common	Headache
	Uncommon	Dizziness, lethargy Paraesthesia, dysgeusia, hypoaesthesia
Gastrointestinal disorders	Very common	Nausea, vomiting
	Uncommon	Diarrhoea, abdominal pain
Skin and subcutaneous tissue disorders	Uncommon	Hyperhidrosis, rash
	Rare	Urticaria
Musculoskeletal and connective tissue disorders	Very common	Myalgia
	Uncommon	Pain in extremity, muscle spasms, arthralgia
General disorders and administration site conditions	Very common	Fatigue Injection site pain
	Common	Injection site pruritus, induration, swelling, erythema Pyrexia

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 <https://coronavirus-yellowcard.mhra.gov.uk/> or search for MHRA Yellow Card in the Google Play or Apple App Store and include the vaccine brand and batch/Lot number if available.

Alternatively, adverse events of concern in association with COVID-19 Vaccine Valneva can be reported to Valneva Austria GmbH on +43676845567 361 or email to VaccineSafety@valneva.com.

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

4.9 Overdose

No case of overdose has been reported in the clinical studies.

There is no specific treatment for an overdose with COVID-19 Vaccine Valneva. In the event of an overdose, the individual should be monitored and provided with symptomatic treatment as appropriate.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Mechanism of action

COVID-19 Vaccine Valneva is a highly purified, inactivated, and adjuvanted whole virus SARS-CoV-2 vaccine. Two adjuvants are added to increase the magnitude of vaccine-mediated immune responses.

Following administration, the spike protein of SARS-CoV-2 as well as other viral surface antigens stimulate both neutralising and other functional binding antibodies, as well as cellular immune responses (Th1) directed against the spike and other surface proteins, which may contribute to protection against COVID-19.

Immunogenicity

An ongoing pivotal randomised, observer-blind, active-controlled, Phase III superiority study is being conducted in the United Kingdom to investigate the immunogenicity and safety of COVID-19 Vaccine Valneva (VLA2001) compared to Vaxzevria in healthy adults (or with stable medical condition) aged 30 years and older. In total, 2,975 participants were randomised (2:1) to receive either a 2-dose intramuscular immunisation with VLA2001 (n=1,978) or Vaxzevria (n=997) to be administered 28 days apart. Median age was 34 and 35 years, respectively; overall, less than 1% of the population studied was older than 50 years. Both arms included slightly more male (57%) than female (43%) participants and 93% were White. The vast majority of participants were seronegative for COVID-19 at screening using a rapid antibody test (94.5% in the VLA2001 arm and 96.8% in the Vaxzevria arm. The second vaccine dose was administered with a median interval of 29 days (range 23 to 64) after the first dose.

Samples from 990 participants (n=492 VLA2001 and n=498 Vaxzevria) with no neutralising antibodies at baseline were considered in the primary immunogenicity analysis. The co-primary immunogenicity endpoints were geometric mean titres (GMT) and seroconversion rates (SCR; defined as a 4-fold increase from baseline) of SARS-CoV-2-specific neutralising antibodies measured two weeks after the second dose (i.e., Day 43). The objective of the trial was to demonstrate superiority of GMTs for VLA2001 compared to Vaxzevria and non-inferiority for SCRs (with a margin of -10% for the difference). The results are shown in Table 1.

Table 1: SARS-CoV-2 neutralising antibodies (ND50) on Day 43

Parameter	VLA2001 (n=492)	Vaxzevria (n=498)	Comparison
GMT			
N	492	493	
GMT (95% CI)	803.5 (748.48, 862.59)	576.6 (543.59, 611.66)	
Median	867.0	553.0	
Min, Max	31, 12800	66, 12800	
GMT Ratio (95% CI)			1.39 (1.25, 1.56)
p-value			<0.0001
SCR			
N	456	449	
SCR n (%)	444 (97.4)	444 (98.9)	
95% CI	(0.954, 0.986)	(0.974, 0.996)	
Difference 95% CI			-0.015 (-0.033, 0.002)

GMT: Geometric mean titre, GMT ratio: GMT VLA2001/GMT Vaxzevria, CI: Confidence interval

SCR: Seroconversion rate defined as ≥ 4 -fold increase in SARS-CoV-2-specific neutralising antibody titre levels between Day 1 and day 43; difference VLA2001-Vaxzevria

Before the second vaccine dose, i.e., 4 weeks after the first dose (Day 29), GMTs (95% CI) measured in a subset of 235 samples were 68.6 (60.3, 78.0) after VLA2001 and 225.7 (201.4, 253.0) after Vaxzevria, with a GMT ratio (95% CI) of 0.30 (0.25, 0.37). These results indicate that the second dose of VLA2001 is necessary to induce robust antibody levels in baseline negative participants and thereby provide protection against COVID-19.

GMTs and SCRs of anti-spike binding IgG antibodies (measured by ELISA) showed similar trends to neutralising antibodies at Days 29 and 43.

Cellular immune response was investigated using an interferon gamma T-cell ELISpot[®] assay against the spike, nucleocapsid and membrane proteins. The response against the spike protein (spot forming units per 2.5×10^5 peripheral blood mononuclear cells) tended to be lower for VLA2001 (median 10; range 0-152) compared to Vaxzevria (median 20; range 2-130) on Day 43. In contrast, a response against the nucleocapsid and membrane proteins was apparent for VLA2001, which did not exist for Vaxzevria.

An additional cohort of 1,042 participants aged 18 – 29 years received VLA2001 in an open-label fashion. Anti-spike IgG GMT (95% CI) was higher in this group (3033 [2628, 3500]) than in the older (≥ 30 years) group (2331 [2113, 2573]).

Paediatric population

The licensing authority has deferred the obligation to submit the results of studies with COVID-19 Vaccine Valneva in 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 licensing authority 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 repeat dose toxicity and reproductive and developmental toxicity.

General toxicity

Intramuscular administration of VLA2001 (inactivated whole virus vaccine produced on Vero cells) on three occasions at 2 weekly intervals to rats was well tolerated. All observations were considered physiological or immunological responses to the vaccine.

Reproductive toxicity

In a reproductive toxicology study in female rats VLA2001 did not affect reproductive parameters, delivery or fetal development. The vaccine was administered by intramuscular injection twice prior to mating and on gestation day 6.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dulbecco’s Phosphate Buffer Saline (DPBS) consisting of:

Sodium chloride

Sodium phosphate dibasic anhydrous

Potassium phosphate mono anhydrous (E340)

Potassium chloride (E508)
Water for injections

Recombinant human albumin (rHA) containing:

Sodium
Octanoate
Polysorbate 80
Water for injections

For adjuvant, see section 2.

6.2 Incompatibilities

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

6.3 Shelf life

Unopened multi-dose vial

12 months when stored in a refrigerator (2°C to 8°C)

After first opening

6 hours
Do not freeze.

Chemical and physical in-use stability of the vaccine has been demonstrated for 6 hours in vial when stored at room temperature. After this time, the vial must be discarded.

The COVID-19 Vaccine (inactivated, adjuvanted) Valneva does not contain any preservatives. Aseptic technique should be used to withdraw doses from the multi-dose vial. From a microbiological point of view, after first dose withdrawal the vaccine should be used as soon as practically possible and within 6 hours.

Once opened and after first dose withdrawal the multi-dose vial should be marked with discarding date and time.

6.4 Special precautions for storage

Unopened multi-dose vial

Store in a refrigerator at 2°C to 8°C.
Do not freeze.
Store vials in the original package in order to protect from light.

For storage conditions after first opening of the vaccine, see section 6.3.

6.5 Nature and contents of container and special equipment for use, administration or implantation

Multi-dose vial (type I glass) with a stopper (flurotec-coated bromobutyl) and a flip-off plastic cap with aluminium seal containing 5 mL suspension for injection (10 doses of each 0.5 mL).

Pack size: 10 multi-dose vials.

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 each dose.

Storage and handling

- The vaccine comes ready to use.
- Unopened multi-dose vial should be stored at 2°C to 8°C.
- The vaccine may be stored between 2°C to 25°C when in use.
- Invert multiple times before use to form a uniform suspension. Do not shake.
- The vaccine should be inspected visually for foreign particulate matter and discolouration prior to administration. Discard if discoloured or containing foreign particulate matter.
- COVID-19 Vaccine Valneva must not be mixed with other medicinal products or diluted in the same syringe.

Administration

- Use aseptic techniques, cleanse vial stopper with a single-use antiseptic swab.
- Use a separate sterile administration needle and syringe for each individual.
- Use a low-dead volume syringe and/or needle combination, for which the combined dead volume is $\leq 30 \mu\text{L}$, in order to extract 10 doses. The device should be compatible for intramuscular injection, with a needle of 21 gauge or narrower.
- If a syringe and needle combination is used, for which the combined dead volume is above $30 \mu\text{L}$, less than ten doses can be extracted.
- Withdraw 0.5 mL of the vaccine.
- The preferred injection site is the muscle of the upper arm.
- If the amount of vaccine remaining in the vial cannot provide a full dose of 0.5 mL, discard the vial and any excess volume.
- Do not pool excess vaccine from multiple vials.

Disposal

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

7. MARKETING AUTHORISATION HOLDER

Valneva Austria GmbH
Campus Vienna Biocenter 3
1030 Vienna
Austria

8. MARKETING AUTHORISATION NUMBER(S)

PL 43185/0002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14 April 2022

10. DATE OF REVISION OF THE TEXT