

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

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

This is a multi-dose vial which contains 10 doses of 0.5 mL

One dose (0.5 mL) contains 33 Antigen Units (AgU) of inactivated SARS-CoV-2 virus^{1,2,3}.

¹ Wuhan strain hCoV-19/Italy/INMI1-isl/2020

² Produced on Vero cells (African green monkey cells)

³ Adsorbed on aluminium hydroxide (0.5 mg Al³⁺ in total) and adjuvanted by 1 mg CpG 1018 (cytosine phospho-guanine) in total.

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 (inactivated, adjuvanted) Valneva is indicated for active immunisation to prevent COVID-19 caused by SARS-CoV-2 in individuals 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 18 to 50 years of age

COVID-19 Vaccine (inactivated, adjuvanted) Valneva is administered intramuscularly as a course of 2 doses of 0.5 mL each. The second dose should be administered 28 days after the first dose (see sections 4.4 and 5.1).

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

Paediatric population

The safety and immunogenicity of COVID-19 Vaccine (inactivated, adjuvanted) 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.

Method of administration

COVID-19 Vaccine (inactivated, adjuvanted) Valneva should be administered intramuscularly. The preferred site is the deltoid muscle of the upper arm (preferably the non-dominant arm).

Do not inject the vaccine intravascularly, subcutaneously or intradermally.

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

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

For instructions 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, or yeast-derived residues (i.e. yeast DNA, yeast antigens and mannosylated rHA) of the manufacturing process of the recombinant human albumin (rHA).

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

Events of anaphylaxis have been reported with COVID-19 vaccines. Appropriate medical treatment and supervision should always be readily available in case of anaphylactic reaction following administration of the vaccine.

Close observation for at least 15 minutes is recommended following vaccination. A second dose of the vaccine should not be given to those who have experienced anaphylaxis to the first dose of COVID-19 Vaccine (inactivated, adjuvanted) Valneva.

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 to 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 (inactivated, adjuvanted) Valneva may be lower in immunosuppressed individuals.

Duration of protection

The duration of protection afforded by the vaccine is unknown as it is still being determined by ongoing clinical studies.

Limitations of vaccine effectiveness

Individuals may not be fully protected until 14 days after their second dose. As with all vaccines, vaccination with COVID-19 Vaccine (inactivated, adjuvanted) Valneva may not protect all vaccine recipients (see section 5.1).

Excipients

Potassium

This vaccine contains potassium, less than 1 mmol (39 mg) per 0.5 mL dose, that is to say essentially 'potassium-free'.

Sodium

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 (inactivated, adjuvanted) Valneva with other vaccines has not been studied.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is no experience with use of COVID-19 Vaccine (inactivated, adjuvanted) Valneva 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 (inactivated, adjuvanted) Valneva 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 (inactivated, adjuvanted, adsorbed) Valneva 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 (inactivated, adjuvanted) 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 (inactivated, adjuvanted) Valneva (VLA2001) was evaluated from an interim analysis of an ongoing study in the United Kingdom in adult healthy participants (or with a stable medical condition) aged 18 years and older. 2,972 subjects were randomized to receive either VLA2001 (n=1,977) or the comparator AZD1222 (n=995) in a blinded manner, while 1,040 subjects from 18-30 years of age received open label VLA2001. The median age of the participants was 33 years, with less than 1% above 50 years.

The most frequently reported adverse reactions in the pivotal studies were injection site tenderness (76,4%), fatigue (57,3%), injection site pain (52,9%), headache (40,6%), myalgia (44,0%), and nausea/vomiting (14,8%). 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 the available data)

Table 1. Adverse reactions from pivotal clinical study

MedDRA system organ class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Uncommon	Lymphadenopathy
	Rare	Thrombocytopenia
Nervous system disorders	Very common	Headache
	Uncommon	Dizziness, paraesthesia, dysgeusia, syncope, hypoaesthesia, migraine
Eye disorders	Rare	Photophobia
Vascular disorders	Rare	Thrombophlebitis
Respiratory, thoracic, and mediastinal disorders	Common	Oropharyngeal pain
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 tenderness, injection site pain
	Common	Injection site pruritus, injection site induration, injection site swelling, injection site erythema, pyrexia
Investigations	Uncommon	Red blood cell sedimentation rate increased

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in [Appendix V](#) and include batch/lot number if available.

4.9 Overdose

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

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Mechanism of action

COVID-19 Vaccine (inactivated, adjuvanted) Valneva (VLA2001) is a purified, inactivated, and adjuvanted whole virus SARS-CoV-2 (Wuhan strain hCoV-19/Italy/INMI1-isl/2020) vaccine grown on Vero cells.

The vaccine manufacturing process makes the virus unable to replicate and delivers intact spike proteins on the virus surface. Adjuvants are added to increase the magnitude of vaccine-mediated immune responses.

Following administration, VLA2001 induces SARS-CoV-2 neutralising antibodies, as well as cellular immune responses (Th1) directed against the spike and other surface proteins, which may contribute to protection against COVID-19. Using this vaccine, the cellular immune response is thus not limited to the S-protein but also directed against other SARS-CoV-2 surface antigens. No data on induction of humoral immune responses directed against SARS-CoV-2 antigens other than S-protein are available in humans.

Pharmacodynamic effects

Immunogenicity

Efficacy of COVID-19 Vaccine (inactivated, adjuvanted) Valneva (VLA2001) has been inferred by immunobridging of immune responses to the authorized ChAdOx1-S (recombinant) COVID-19 vector vaccine, for which vaccine efficacy has been established.

Pivotal study VLA2001-301

The immunogenicity of COVID-19 vaccine Valneva is being evaluated in one ongoing pivotal randomised, observer-blind, active-controlled, Phase 3 superiority study conducted in the UK to investigate the immunogenicity and safety of VLA2001 against COVID-19 if compared to COVID-19 Vaccine (ChAdOx1-S [recombinant]) (authorised COVID-19 vector vaccine) in adult healthy participants (or with stable medical condition) of either gender aged 18 years and older. In total 4,181 participants were screened, 2,975 participants (≥ 30 years) were randomised (2:1) to receive either a 2-dose immunisation schedule of VLA2001 (n=1,978) or COVID-19 Vaccine (ChAdOx1-S [recombinant]) (n=997) each 28 days apart. Additionally, 1,042 participants aged 18 – 29 years were enrolled in a non-randomised treatment group to receive VLA2001 in an open-label fashion. Immunogenicity and safety will be assessed up to month 12 after the first vaccination.

Demographic and baseline characteristics

The immunogenicity population (IMM) was defined to include all randomised and vaccinated participants of the IMM subset for the primary endpoint evaluation, who were SARS-CoV-2 seronegative and had at least one evaluable post-baseline antibody titre measurement after vaccination. For immunogenicity analyses, samples from 990 participants of the randomised study part (n=492 VLA2001 and n=498 COVID-19 Vaccine (ChAdOx1-S [recombinant])) seronegative at baseline have been analysed. Mean age in the IMM population was 36.1 years for VLA2001 group and 35.8 years for ChAdOx1-S [recombinant] group. Both groups included more male than female participants (55.3% vs. 44.3% in the VLA group, 58.8% vs. 41.2% in the ChAdOx1-S [recombinant] group). The majority in both treatment groups were white (95.1% in the VLA group, 93.6% in the ChAdOx1-S [recombinant] group).

The per protocol (PP) population comprised of all IMM-population participants who had no major protocol violations that impacted the immune response (n=489 VLA2001 and n=498 COVID-19 Vaccine (ChAdOx1-S [recombinant]) participants met the criteria).

Co-primary endpoints

The co-primary immunogenicity endpoints were defined as superiority in terms of geometric mean titres (GMT) in the IMM population as well as non-inferiority of the seroconversion rate (defined as a 4-fold increase from baseline) of SARS-CoV-2-specific neutralising antibodies, two weeks after the second vaccination (i.e., Day 43) in adults aged 30 years and older (PP population).

GMT of neutralising antibodies at Day 43

Table 1 shows GMT of neutralizing antibodies on Day 43 in the Immunogenicity population. All participants included in this analysis had baseline ND50 values below the limit of detection.

Table 1: SARS-CoV-2 neutralising antibodies (ND50) on Day 1 and Day 43; co-primary analysis (IMM population)

Treatment group		VLA2001 (n=492)	COVID-19 Vaccine (ChAdOx1-S [recombinant]) (n=498)	Overall (n=990)
Day 43	n	492	493	985
	GMT (95% CI)	803.5 (748.48, 862.59)	576.6 (543.59, 611.66)	680.6 (649.40, 713.22)
	GMT Ratio (95% CI)			1.39 (1.25, 1.56)
	Median	867.0	553.0	659.0
	Min, Max	31, 12800	66, 12800	31, 12800
	p-value ¹			<0.0001

GMT: Geometric mean titre, GMT ratio: GMT VLA2001/GMT COVID-19 Vaccine (ChAdOx1-S [recombinant]), CI: Confidence interval

¹ p-value and CI calculated using a two-sided t-test applied to log10 transformed data

Seroconversion rates at Day 43

Table 2 shows seroconversion rates on Day 43 in the per-protocol population.

Table 2: Proportion of participants with seroconversion in terms of neutralising antibodies on Day 43 (PP population)

Treatment group	VLA2001 (N=492)	COVID-19 Vaccine (ChAdOx1- S [recombinan t]) (N=498)	Overall (N=990)
Number of patients with eligible samples at visit	456	449	905
Participants with seroconversion at Day 43			
n (%)	444 (97.4)	444 (98.9)	888 (98.1)
95% CI ¹	(0.954,0.986)	(0.974,0.996)	(0.970,0.989)
p-value ²			0.0911
95% CI for Difference ²			(-.033,0.002)

Note: Seroconversion is defined as ≥ 4 -fold increase in SARS-CoV-2-specific neutralising antibody titre levels between Day 1 and post-vaccination sample collection timepoints (for first interim analysis: Day 1 and Day 43). Displayed are only rates at Day 43 (all values at Day 1 are “0”).

CI: Confidence Interval

¹ Exact 95% Clopper-Pearson confidence interval for proportion.

² P value or two-sided CI is for the difference in proportions (VLA2001-COVID-19 Vaccine (ChAdOx1-S [recombinant])) of participants with seroconversion at each particular visit.

When assessed as secondary endpoint GMT-fold increases for neutralising antibodies at Day 43 compared to baseline were 25.9 (95% CI: 24.14, 27.83) in the VLA2001 group and 18.6 (95% CI: 17.54, 19.73) in the COVID-19 Vaccine (ChAdOx1-S [recombinant]) group ($p < 0.0001$) (IMM population, results in PP population similar).

Secondary endpoints

Similar to the neutralising antibodies, a higher GMT of S-protein binding antibodies (IgG ELISA) was observed at Day 43 in the VLA2001 group (GMT 2,361.7 (95% CI: 2,171.08, 2,569.11) compared to the COVID-19 Vaccine (ChAdOx1-S [recombinant]) group (GMT 2,126.4 (95% CI: 1,992.42, 2,269.45)) (IMM population, results in PP population similar). At Day 43, seroconversion in terms of S-protein binding IgG antibodies were 98.0% (95% CI: 0.963,0.990) for VLA2001 and 98.8% (95% CI: 0.974,0.996) for COVID-19 Vaccine (ChAdOx1-S [recombinant]) (IMM population, results in PP population similar). Numbers of participants with ≥ 2 -fold, ≥ 10 -fold and ≥ 20 -fold increase in S-protein binding antibody titre at Day 43 were similar for both treatment groups with nearly 100% for ≥ 2 -fold increase and 90% or more for ≥ 10 -fold and ≥ 20 -fold increase.

Cellular immune response was demonstrated by VLA2001 inducing broad T-cell responses with antigen-specific interferon-gamma producing T-cells reactive (defined as normalised spot forming units ≥ 6 in an interferon gamma T-cell ELISpot test) against the full sequence spike protein in 74.3%, against nucleocapsid protein in 45.9% and against membrane protein in 20.3% of the participants as assessed in the PBMC subset of the IMM population at Day 43 (results in PP population similar).

Antibody responses measured after a single VLA2001 vaccination were lower when compared to two VLA2001 vaccinations. This indicates that the second vaccination with VLA2001 is necessary to induce robust antibody levels in baseline negative participants and thereby provide protection against COVID-19 caused by SARS-CoV-2.

At a mean observation time of 151 days, 87 (8.4%) COVID-19 cases (exploratory endpoint) occurred in participants 18-29 years and 139 (7%) in participants \geq 30 years who received two doses of VLA2001. 60 (6%) cases occurred in participants who received two doses of COVID-19 Vaccine (ChAdOx1-S [recombinant]). All COVID-19 cases were assessed as mild or moderate by the investigator and none of the COVID-19 cases were severe.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with COVID-19 Vaccine (inactivated, adjuvanted) Valneva in one or more subsets of the paediatric population in prevention of COVID-19 (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 repeat dose toxicity and reproduction and developmental toxicity conducted.

Repeat dose toxicity

Intramuscular administration of the vaccine on three occasions at 2 weekly intervals (Days 1, 15 and 29) was well tolerated in rats. The study showed microscopic findings that were still evident after a 3-week treatment free period, but with reduced incidences in the administration sites and spleen compared to before the treatment free period, indicating partial recovery. The observations would be considered physiological and immunological responses to the vaccine.

Genotoxicity/carcinogenicity

Neither genotoxicity nor carcinogenicity studies were performed. The components of the vaccine are not expected to have genotoxic potential.

Reproductive toxicity

A reproductive toxicity trial studying VLA2001 in female Han Wistar rats demonstrated that VLA2001 did not affect the reproductive parameters, the delivery and foetal development. No data are available on vaccine placental transfer or excretion in milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Sodium phosphate dibasic anhydrous (E339)
Potassium phosphate mono anhydrous (E340)
Potassium chloride (E508)
Water for injections

Recombinant human albumin (rHA) produced in yeast (*Saccharomyces cerevisiae*)

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

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

After first opening

- either up to 6 hours when stored below 25°C
- or up to 48 hours when stored at 2-8°C with a maximum time of 2.5 hours at room temperature (15-25°C)

Do not freeze.

Chemical and physical in-use stability of the vaccine has been demonstrated for 6 hours in vial when stored below 25°C or up to 48 hours when stored at 2-8°C with a maximum time of 2.5 hours at room temperature (15-25°C). After this time, the vial must be discarded.

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 opening (first needle puncture) the vaccine 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

Unopened multi-dose vial

Store in a refrigerator (2°C to 8°C).

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Unopened COVID-19 Vaccine (inactivated, adjuvanted) Valneva is stable for a total of 6 hours at 25°C. This is not a recommended storage or shipping condition but may guide decisions for use in case of temporary temperature excursions during the storage at 2°C -8°C.

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

6.5 Nature and contents of container

5 mL suspension for injection in a multidose vial (type I glass) with a stopper (flurotec-coated bromobutyl) and a flip-off plastic cap with aluminium seal.

Each vial contains 10 doses of 0.5 mL each.

Pack size: 10 multidose 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 for use.
- Unopened multidose vial should be stored at 2°C to 8°C, keep the vial in the outer carton in order to protect from light.
- The vaccine may be stored between 2°C to 25°C when in use.
- After first puncture, use the vaccine within 6 hours when stored below 25°C or up to 48 hours when stored at 2-8°C with a maximum time of 2.5 hours at room temperature (15-25°C). Record the date and time of first puncture on the vial label.
- Discard this vaccine if not used within the above mentioned time frames after first puncture of the vial.

Preparation

- 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 (inactivated, adjuvanted) 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 ≤ 30 microlitres for all doses, in order to extract 10 doses. The device should be compatible for intramuscular injection, with a needle of 21 gauge or narrower.
- If standard syringes and needles are used, for which the combined dead volume is above 30 microlitres, there may not be sufficient volume to extract the tenth dose from a single vial.
- Withdraw 0.5 mL of the vaccine.
- The preferred injection site is the muscle of the upper arm.
- The vaccine must not be administered intravascularly, subcutaneously or intradermally.
- 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)

EU/1/21/1624/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24 June 2022

10. DATE OF REVISION OF THE TEXT

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

ANNEX II

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

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

Valneva Scotland Limited
Oakbank Park Road
Livingston EH53 OTG
Scotland, UK

Or

IDT Biologika GmbH
Am Pharmapark
06861 Dessau-Rosslau
Germany

Name and address of the manufacturer(s) responsible for batch release

Valneva Sweden AB
Gunnar Asplunds Allé 16
171 69 Solna
Sweden

Or

Valneva Austria GmbH
Campus Vienna Biocenter 3
1030 Vienna
Austria

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

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

- **Official batch release**

In accordance with Article 114 of Directive 2001/83/EC, the official batch release will be undertaken by a state laboratory or a laboratory designated for that purpose.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

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

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

CARTON BOX

1. NAME OF THE MEDICINAL PRODUCT

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

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each vial contains 10 doses of 0.5 mL
One dose (0.5 mL) contains 33 Antigen Units (AgU) of inactivated SARS-CoV-2, adsorbed on aluminium hydroxide (0.5 mg Al³⁺), adjuvanted with CpG 1018 (1 mg).

3. LIST OF EXCIPIENTS

Excipients: Sodium chloride, sodium phosphate dibasic anhydrous, potassium phosphate mono anhydrous, potassium chloride, water for injections and recombinant human albumin.

4. PHARMACEUTICAL FORM AND CONTENTS

Suspension for injection
10 multidose vials

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.
For more information scan the code with a mobile device or visit www.covid19-vaccine-valneva.com.



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

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Invert multiple times before use to form a uniform suspension.
Do not shake.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

After first puncture, use the vaccine within 6 hours when stored below 25°C or up to 48 hours when stored at 2-8°C with a maximum time of 2.5 hours at room temperature (15-25°C).

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

Valneva Austria GmbH
Campus Vienna Biocenter 3
1030 Vienna
Austria

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1624/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN

NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

MULTI-DOSE VIAL

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

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

2. METHOD OF ADMINISTRATION

IM

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 doses of 0.5 mL

6. OTHER

Date:

Time:

B. PACKAGE LEAFLET

Package leaflet: Information for the user

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

- 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 COVID-19 Vaccine (inactivated, adjuvanted) Valneva is and what it is used for
2. What you need to know before you are given COVID-19 Vaccine (inactivated, adjuvanted) Valneva
3. How COVID-19 Vaccine (inactivated, adjuvanted) Valneva is given
4. Possible side effects
5. How to store COVID-19 Vaccine (inactivated, adjuvanted) Valneva
6. Contents of the pack and other information

1. What COVID-19 Vaccine (inactivated, adjuvanted) Valneva is and what it is used for

COVID-19 Vaccine (inactivated, adjuvanted) Valneva is a vaccine used to prevent COVID-19 caused by SARS-CoV-2.

COVID-19 Vaccine (inactivated, adjuvanted) Valneva is given to adults 18 to 50 years of age.

The vaccine causes the immune system (the body's natural defences) to produce antibodies and blood cells that works against the virus so giving protection against COVID-19.

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

2. What you need to know before you are given COVID-19 Vaccine (inactivated, adjuvanted) Valneva

COVID-19 Vaccine (inactivated, adjuvanted) Valneva must not be given

- if you are allergic to the active substance, to yeast or yeast-derived components, 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 COVID-19 Vaccine (inactivated, adjuvanted) Valneva if:

- you have previously had a severe or life-threatening allergic reaction after any other vaccine injection or after you were given COVID-19 Vaccine (inactivated, adjuvanted) Valneva in the past
- you have ever fainted following any needle injection or if you have anxiety related to injections
- you have a severe illness or infection with high fever. You can have your vaccination if you have a mild fever or upper airway infection like a cold

- you have a problem with bleeding, you bruise easily or if you use a medicine to prevent blood clots
- your immune system does not work properly (immunodeficiency) or you are taking medicines that weaken the immune system (such as high-dose corticosteroids, immunosuppressants, or cancer medicines).

As with any vaccine, the 2-dose vaccination course of COVID-19 Vaccine (inactivated, adjuvanted) Valneva may not fully protect all those who receive it and it is not known how long you will be protected.

Children and adolescents

COVID-19 Vaccine (inactivated, adjuvanted) Valneva is not recommended for children and adolescents aged below 18 years. Currently there is not enough information available on the use of COVID-19 Vaccine (inactivated, adjuvanted) Valneva in children and adolescents younger than 18 years of age.

Other medicines and COVID-19 Vaccine (inactivated, adjuvanted) Valneva

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines or other vaccines.

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 receive this vaccine.

Driving and using machines

Some of the side effects of COVID-19 Vaccine (inactivated, adjuvanted) Valneva listed in section 4 may temporarily affect your ability to drive and use 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.

COVID-19 Vaccine (inactivated, adjuvanted) Valneva contains potassium and sodium

This vaccine contains potassium, less than 1 mmol (39 mg) per 0.5 mL dose, that is to say 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'.

3. How COVID-19 Vaccine (inactivated, adjuvanted) Valneva is given

COVID-19 Vaccine (inactivated, adjuvanted) Valneva is given as an injection of 0.5 mL into a muscle of your upper arm.

You will receive 2 injections of the same vaccine, given 28 days apart to complete the vaccination course.

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

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

If you miss the appointment for your 2nd dose of COVID-19 Vaccine (inactivated, adjuvanted) Valneva

- If you miss the appointment, arrange another visit as soon as possible with your doctor, pharmacist or nurse.
- If you miss a scheduled injection, you will not be fully protected against COVID-19.

4. Possible side effects

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

The following side effects may occur with COVID-19 Vaccine (inactivated, adjuvanted) Valneva:

Get **urgent** medical attention if you get any of the following signs and symptoms of an allergic reaction

- feeling faint or light-headed
- changes in your heartbeat
- shortness of breath
- wheezing
- swelling of your lips, face, or throat
- hives or rash
- nausea or vomiting
- stomach pain

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

Very common side effects (may affect more than 1 in 10 people)

- headache
- nausea
- vomiting
- muscle pain
- tiredness
- injection site: tenderness, pain

Common side effects (may affect up to 1 in 10 people)

- throat pain
- injection site: itching, hardening, swelling, redness
- fever

Uncommon side effects (may affect up to 1 in 100 people)

- enlarged lymph nodes
- dizziness
- abnormal sensation of skin (for example pins and needles)
- taste disturbance
- fainting
- reduced sensitivity
- migraine
- diarrhoea
- belly pain
- excessive sweating
- rash
- pain in leg or arm
- joint pain
- muscle cramps
- red blood cell sedimentation rate increased

Rare side effects (may affect up to 1 in 1,000 people)

- low blood platelet count
- sensitivity to light
- vein inflammation related to a blood clot

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](#) and include batch/Lot number if available. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store COVID-19 Vaccine (inactivated, adjuvanted) Valneva

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

This medicine should not be used after the expiry date which is stated on the carton and vial label after “EXP”. The expiry date refers to the last day of that month. Your healthcare professional is responsible for the time and conditions for storing of this vaccine.

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

6. Contents of the pack and other information

What COVID-19 Vaccine (inactivated, adjuvanted) Valneva contains

One dose (0.5 mL) contains 33 Antigen Units (AgU) of inactivated SARS-CoV-2 virus^{1,2,3}.

¹ Wuhan strain hCoV-19/Italy/INMI1-isl/2020

² Produced on Vero cells (African green monkey cells)

³ Adsorbed on aluminium hydroxide (0.5 mg Al³⁺ in total) and adjuvanted by 1 mg CpG1018 (cytosine phospho-guanine) in total.

One multidose vial contains 10 doses of 0.5 mL.

The other ingredients are: sodium chloride, sodium phosphate dibasic anhydrous (E339), potassium phosphate mono anhydrous (E340), potassium chloride (E508), water for injections and recombinant human albumin (rHA).

COVID-19 Vaccine (inactivated, adjuvanted) Valneva contains potassium and sodium (see section 2).

What COVID-19 Vaccine (inactivated, adjuvanted) Valneva looks like and contents of the pack

White to off-white suspension for injection (injection) in a glass multi-dose vial closed with rubber stopper and a flip-off plastic cap with aluminium seal.

Pack size: 10 multi-dose vials

Marketing Authorisation Holder

Valneva Austria GmbH
Campus Vienna Biocenter 3
1030 Vienna
Austria

Manufacturers

Valneva Sweden AB
Gunnar Asplunds Allé 16
171 69 Solna
Sweden

Or

Valneva Austria GmbH
Campus Vienna Biocenter 3
1030 Vienna,
Austria

For any information about this medicine, please contact the Marketing Authorisation Holder by the following email-address: covid19@valneva.com

This leaflet was last revised in

Other sources of information

For more information scan the QR code with a mobile device to get this package leaflet in different languages or visit:

www.covid19-vaccine-valneva.com



Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>

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

The following information is intended for healthcare professionals only:

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Storage conditions

Store in a refrigerator at 2°C to 8°C.

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Shelf life

Unopened vial

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

Unopened COVID-19 Vaccine (inactivated, adjuvanted) Valneva is stable for a total of 6 hours at 25°C. This is not a recommended storage or shipping condition.

After first opening

6 hours when stored below 25°C or up to 48 hours when stored at 2-8°C with a maximum time of 2.5 hours at room temperature (15-25°C).
Do not freeze.

Chemical and physical in-use stability of the vaccine has been demonstrated in the vial for 6 hours when stored below 25°C or up to 48 hours when stored at 2-8°C with a maximum time of 2.5 hours at room temperature (15-25°C) . 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 multidose vial. From a microbiological point of view, after first opening (first needle puncture), the vaccine should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Handling and administration

The vaccine should be prepared and administered by a trained healthcare professional using aseptic techniques to ensure sterility of the suspension.

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

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

- The vaccine comes ready for use.
- Unopened multi-dose vial should be stored at 2°C to 8°C, keep the vial in the outer carton in order to protect from light.
- The vaccine may be stored between 2°C to 25°C when in use.
- After first puncture use within 6 hours when stored below 25° or use within 48h when stored at 2-8°C with a maximum time of 2.5h at room temperature (15-25°C). Record the date and time of first puncture on the vial label.
- Discard this vaccine if not used within the above mentioned time frames after first puncture of the vial.
- Invert multiple times before use to form a uniform suspension. Do not shake
- The vaccine should be inspected visually for foreign particulate matter and discoloration prior to administration. Discard if discoloured or containing foreign particulate matter.
- COVID-19 Vaccine (inactivated, adjuvanted) Valneva must not be mixed with other medicinal products or diluted in the same syringe.
- Use aseptic technique, 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 ≤ 30 microlitres for all doses, in order to extract 10 doses. The device should be compatible for intramuscular injection, with a needle of 21 gauge or narrower.
- If standard syringes and needles are used, for which the combined dead volume is above 30 microlitres, there may not be sufficient volume to extract 10 doses from a single vial.
- Withdraw 0.5 mL of the vaccine.
- The preferred injection site is the muscle of the upper arm.
- Do not administer the vaccine intravascularly, subcutaneously or intradermally.
- 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.