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

IXCHIQ powder and solvent for solution for injection
Chikungunya vaccine (live)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, one dose (0.5 ml) contains:
Chikungunya virus (CHIKV) Δ5nsP3 strain (live, attenuated)* not less than 3.0 $\log_{10}$ $TCID_{50}$**

* Produced in Vero cells
** 50% tissue culture infectious dose

This product contains genetically modified organisms (GMOs)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

Before reconstitution, the lyophilized vaccine is a white to slightly yellowish homogeneous powder. The solvent is a clear colourless liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

IXCHIQ is indicated for active immunisation for the prevention of disease caused by chikungunya virus (CHIKV) in individuals between 12 and 64 years old.

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

4.2 Posology and method of administration

Posology

Individuals from 12 years of age

IXCHIQ is administered as a single dose of 0.5 mL.

Revaccination (Booster dose)

The need for revaccination has not been established.

Paediatric population aged less than 12 years

The safety and immunogenicity of IXCHIQ in children aged less than 12 years have not been established. No data are available for children below 12 years of age.

Method of administration

For intramuscular injection only, after reconstitution.

IXCHIQ should be administered intramuscularly in the deltoid muscle within 2 hours of reconstitution.
The vaccine should not be mixed in the same syringe with any other vaccines or medicinal products.
For instructions on reconstitution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

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

Immunodeficient or immunosuppressed individuals due to disease or medical therapy (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, long-term immunosuppressive therapy or patients with HIV infection who are severely immunocompromised).

Individuals aged 65 years and older

4.4 Special warnings and precautions for use

Traceability

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

Hypersensitivity and anaphylaxis

Appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine. Close observation for at least 15 minutes is recommended following vaccination.

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

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 injection in these individuals.

Limitations of vaccine effectiveness

The ability of IXCHIQ to prevent disease due to chikungunya virus was based on a serological surrogate endpoint (see section 5.1). As with any vaccine, a protective immune response may not be elicited after vaccination in all persons. It is recommended to continue personal protection measures against mosquito bites after vaccination.

Pregnancy

A decision to administer IXCHIQ during pregnancy should take into consideration the individual's risk of wild-type CHIKV infection, gestational age, and risks to the foetus or neonate from vertical transmission of wild-type CHIKV (see section 4.6).

Blood donation

Vaccine viraemia was detected in 90% of subjects 3 days after vaccination, proportions of vaccinees with detectable virus declined to 17% by 7 days after administration of IXCHIQ and no vaccine viraemia was detected 15 days after vaccination. See sections 4.6 and 4.8.
Individuals administered IXCHIQ should not donate blood for at least 4 weeks post-vaccination.

Chikungunya-like Adverse Reactions

IXCHIQ may cause severe or prolonged chikungunya-like adverse reactions (see section 4.8).

Sodium

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

Potassium

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

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant administration with other vaccines

IXCHIQ is not recommended to be co-administered with other vaccines because there are no data on the safety and immunogenicity following concomitant administration of IXCHIQ with other vaccines.

Administration of immune globulins, blood or plasma transfusions 3 months before or up to 1 month after IXCHIQ administration may interfere with the expected immune response.

4.6 Fertility, pregnancy and lactation

Pregnancy

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

There is limited amount of data from the use of IXCHIQ in pregnant women. These data are not sufficient to conclude on the absence of potential effects of IXCHIQ on pregnancy, embryo-foetal development, parturition and post-natal development.

Vertical transmission of wild-type CHIKV from pregnant individuals with viraemia at delivery is common and can cause potentially fatal CHIKV disease in neonates. Vaccine viraemia occurs in the first week following administration of IXCHIQ, with resolution of viraemia by 14 days after vaccination. It is not known if the vaccine virus can be vertically transmitted and cause foetal or neonatal adverse reactions.

Decisions to administer IXCHIQ during pregnancy should take into consideration the individual's risk of exposure to wild-type CHIKV, gestational age, and risks to the foetus or neonate from vertical transmission of wild-type CHIKV.

Breast-feeding

It is unknown if IXCHIQ is excreted in human milk. A risk to the breastfed child cannot be excluded. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for IXCHIQ and any potential adverse effects on the breastfed child from IXCHIQ.

Animal studies did not indicate any direct or indirect harmful effects with respect to lactation (see section 5.3).

Fertility

No specific studies have been performed on fertility.

Animal studies did not indicate any harmful effects with respect to female fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

IXCHIQ 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

Adults ≥ 18 years of age
The overall safety of IXCHIQ is based on an analysis of the pooled safety data from three completed phase I and III clinical studies conducted in the US on 3 610 participants ≥18 years old who received one dose of IXCHIQ with a follow-up of 6 months.

The most common vaccination site reactions were tenderness (10.8%) and pain (6.1%). The most common systemic adverse reactions were headache (32%), fatigue (29.4%), myalgia (23.7%), arthralgia (16.6%), fever (13.8%) and nausea (11.4%).

Adolescents 12 to <18 years of age
Safety in adolescent participants 12 to <18 years was assessed in 502 participants in Brazil who received one dose of IXCHIQ with a follow-up of 6 months. 18.7% of the participants had pre-existing antibodies against chikungunya virus (94 adolescents).

The most common vaccination site reactions in adolescents 12 to <18 years of age were tenderness (19.9%) and pain (19.3%). The most common systemic adverse reactions were headache (51.0%), myalgia (26.9%), fever (24.1%), fatigue (22.3%), nausea (15.9%) and arthralgia (12.9%).

Baseline seropositive adolescents
The proportion of participants that experienced solicited systemic AEs was higher in baseline seronegative participants vaccinated with IXCHIQ than in baseline seropositive participants

vaccinated with IXCHIQ (67.9% and 44.7% respectively). The proportion of participants who experienced solicited local AEs and unsolicited AEs was similar in the IXCHIQ arms of each stratum.

Laboratory parameters

Adults ≥ 18 years of age
The most common abnormal laboratory parameters were neutropenia (41.8%), leukopenia (31.2%), lymphopenia (22.3%), Alanine aminotransferase increased (ALT: 15.5%), and Aspartate aminotransferase increased (AST: 11.7%) (based on an immunogenicity subset of 372 IXCHIQ recipients).

Adolescents 12 to <18 years
The most common abnormal laboratory parameters were neutropenia (40.2%), leukopenia (16.8%), and lymphopenia (11.6%) (based on an immunogenicity subset of 328 IXCHIQ recipients).

Vaccine Viraemia and Shedding

Vaccine virus was demonstrated to be present in blood and urine and might be present in other body fluids. Vaccine viraemia and shedding (measured by genomic amplification methods) following vaccination with IXCHIQ was assessed in one adult clinical trial (VLA1553-101). Viraemia was detected in 90% of subjects 3 days after vaccination, proportions of vaccinees with detectable virus declined to 17% by 7 days after administration of IXCHIQ and no vaccine viraemia was detected 15 days after vaccination. A single participant shed vaccine virus in urine 7 days after vaccination.

Tabulated list of adverse reactions

Adverse reactions are listed according to the following frequency categories:
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 the adverse reactions are presented in the order of decreasing seriousness.

Table 1. Adverse reactions in individuals 12 years of age and older

System organ class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Common	Lymphadenopathy[a]
Endocrine disorders	Rare	Hypovolaemic hyponatraemia[a]
Nervous system disorders	Very common	Headache
	Common	Dizziness[b]
	Uncommon	Paraesthesia
Eye disorders	Common	Eye pain[b]
	Uncommon	Conjunctival hyperaemia[c]
Ear and labyrinth disorders	Uncommon	Tinnitus[a]
Respiratory, thoracic and mediastinal disorders	Uncommon	Dyspnoea
Gastrointestinal disorders	Very common	Nausea
	Common	Vomiting, diarrhoea

Skin and subcutaneous tissue disorders	Common	Rash
	Uncommon	Hyperhidrosis[a]
Musculoskeletal and connective tissue disorders	Very common	Myalgia, arthralgia
	Common	Back pain[a]
General disorders and administration site conditions	Very common	Fatigue, fever, vaccination site reactions (tenderness, pain, erythema, induration, swelling)
	Common	Chills
	Uncommon	Asthenia[a], oedema peripheral[a]
Investigations	Very common	White blood cell count decreased[d]; liver function test increased[a,e]

a. reported in adults only, not reported in adolescents
b. eye pain and dizziness: common in adolescents, uncommon in adults
c. reported in adolescents only, not reported in adults
d. includes: leukopenia (leukocyte decreased), neutropenia (neutrophil decreased) and lymphopenia (lymphocyte decreased).
e. includes: Alanine aminotransferase increased (ALT) and Aspartate aminotransferase increased (AST).

Chikungunya-like Adverse Reactions

Adults
The occurrence of certain adverse event combinations, referred to as chikungunya-like adverse reactions, was retrospectively evaluated in the pooled safety data from phase I and III clinical studies (N=3 610). Chikungunya-like adverse reactions were broadly defined, i.e. occurrence of fever (≥38°C) and at least one other symptom also reported for acute-stage chikungunya illness, including arthralgia or arthritis, myalgia, headache, back pain, rash, lymphadenopathy, and certain neurological, cardiac or ocular symptoms; within 30 days after vaccination, regardless of time of onset, severity or duration of the individual symptoms.
Adverse event combinations qualifying as chikungunya-like adverse reactions were reported in 12.1% of participants. Among those, combinations of fever with headache, fatigue, myalgia or arthralgia were the most common, all other symptoms were reported in fewer than 10% of chikungunya-like adverse reactions. The reported symptoms were mostly mild, 1.8% of participants reported at least one severe symptom, most commonly fever or arthralgia. Median onset of chikungunya-like adverse reactions was 3 days after vaccination, and median time to resolution was 4 days. Longer-lasting symptoms ≥30 days occurred in 0.4% of participants.

Adolescents 12 to <18 years of age
The occurrence of chikungunya-like adverse reactions in adolescents (12 to <18 years) was evaluated in a post-hoc analysis of 502 participants from the phase III study in adolescents. Chikungunya-like adverse reactions in adolescents were defined as fever (≥37.8°C/ 100.0°F) and at least one other symptom also reported for acute-stage chikunguna illness, including arthralgia or arthritis, myalgia, headache, or certain neurological or ocular symptoms, rash, or certain skin symptoms; within 30 days after vaccination, regardless of time of onset, severity or duration of the individual symptoms.
Chikungunya-like adverse reactions were reported in 23.1% of adolescents. Among those, combinations of fever with headache, myalgia, fatigue or arthralgia were the most common, all other symptoms were reported in fewer than 10% participants. 3.6% of participants reported at least one severe symptom, most commonly fever or headache. Median onset of chikungunya-like adverse reactions was 2 days after vaccination, and median time to resolution was 4 days. There were no longer-lasting chikungunya-like adverse reactions reported in adolescents (i.e., at least one symptom with duration ≥30 days).

Baseline seropositive adolescents

The proportion of participants that experienced chikungunya-like adverse reactions was higher in baseline seronegative participants than in baseline seropositive participants vaccinated with IXCHIQ .

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

No case of overdose has been reported in 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: Other viral vaccines, ATC code: Not yet assigned

Mechanism of action

IXCHIQ contains live-attenuated CHIKV of the ECSA/IOL genotype. The exact mechanism of protection against CHIKV infection and/or disease has not been determined. IXCHIQ elicits neutralising antibodies against CHIKV.

Immunogenicity

No efficacy data are available for IXCHIQ. The clinical efficacy of IXCHIQ was inferred from a post-vaccination CHIKV-specific neutralizing antibody titre threshold.

A threshold of CHIKV-specific neutralizing antibody µPRNT50 titre of ≥150 was selected as surrogate marker for protection, referred to as seroresponse. This threshold was determined from a non-human primate passive transfer study in which animals with titres ≥150 were protected against wild-type CHIKV infections and had undetectable virus in blood during 14 days after the challenge. In addition, the threshold was supported by data obtained from a prospective human sero-epidemiological study.

VLA1553-301 was a placebo-controlled study assessing the immunogenicity and safety in generally healthy individuals 18 years and above. The study was conducted in the US. Participants in this study were followed up for 6 months after immunization. The proportion of participants with CHIKV-specific antibody titers ≥150 µPRNT50, i.e. seroresponse rate, 28 days post-vaccination in the CHIKV participants negative for CHIKV neutralizing antibodies of the IXCHIQ arm was the primary endpoint.

Humoral immune response was evaluated in 362 participants (266 in the IXCHIQ arm and 96 in the Placebo arm). All these participants were negative at baseline (pre-vaccination) for CHIKV neutralizing antibodies. The study population included 82 participants 65 years of age or above (59 and 23 in the IXCHIQ and Placebo arm).

VLA1553-321 was a placebo-controlled study assessing the immunogenicity and safety in generally healthy adolescents 12 to <18 years of age. The study was conducted in Brazil which is an endemic country for chikungunya. Participants in this study were followed up to 6 months after immunization. The primary endpoint was similar as in study VLA1553-301.

Humoral immune response was evaluated in 351 participants (303 in the IXCHIQ arm and 48 in the placebo arm). 293 participants were negative, and 58 participants were positive at baseline (pre-vaccination) for CHIKV neutralizing antibodies.

Antibody persistence is evaluated in study VLA1553-303 (follow up of a subset of participants of study of VLA1553-301). Data are available up to 2 years post-immunization. In study VLA1553-321 a subset of adolescents 12 to <18 years of age will be followed for up to 1 year post-immunization.

Seroresponse rate

Adults
In the pivotal trial VLA1553-301, 98.9% of the participants who were administered IXCHIQ presented CHIKV-specific neutralizing antibody titers ≥150 µPRNT50 at 28 days post-vaccination. This percentage was sustained up to 6 months post-vaccination (96.3%). Refer to Table 2. Only 1.6% (n=4/251) of the participants vaccinated with IXCHIQ had CHIKV-specific neutralizing antibody titers ≥150 µPRNT50 at Day 8. No participant had CHIKV-specific neutralizing antibody response ≥150 µPRNT50 in the placebo arm of VLA1553-301.

Table 2. Seroresponse rates over time, as determined by µPRNT$_{50}$ assay, in study VLA1553-301 (PP population)

Study	**VLA1553-301**	
Treatment	Placebo	IXCHIQ
	N=96	N=266
	(n [95%CI])	(n (%) [95%CI])
Baseline day 1	0 (0)	0 (0)
28 days post-vaccination	0 [0.0, 3.8]	263 (98.9) [96.7, 99.8]
6 months post-vaccination	0 [0.0, 4.0]	233 (96.3) [93.1, 98.3]

Abbreviations: CI=confidence interval; µPRNT$_{50}$=50% micro plaque reduction neutralization test; PP=per-protocol (population)

Adolescents 12 to <18 years of age
In the adolescent trial VLA1553-321, 98.8% (248/251) of the CHIKV seronegative participants who were administered IXCHIQ presented CHIKV-specific neutralizing antibody titers ≥150 µPRNT50 at 28 days post-vaccination. This percentage was sustained up to 6 months post-vaccination (99.1% (232/234). 5.7% (n=14/245) of the CHIKV seronegative participants vaccinated with IXCHIQ had CHIKV-specific neutralizing antibody titers ≥150 µPRNT50 at Day 8. The vast majority of CHIKV seropositive participants (50/52) presented CHIKV-specific neutralizing antibody titers ≥150 µPRNT50 before vaccination with IXCHIQ. The percentages remained in the same range 28 days post-vaccination (52/52) and 6 months post-vaccination (45/46).

Table 3. Seroresponse rates over time, as determined by µPRNT$_{50}$ assay, in study VLA1553-321 (PP population)

Study	VLA1553-321			
Treatment	Placebo		IXCHIQ	
	Seronegative N=42	Seropositive N= 6	Seronegative N=251	Seropositive N=52
	(n (%) [95%CI])	(n (%) [95%CI])	(n (%) [95%CI])	(n (%) [95%CI])
Baseline day 1	0 (0)	6 (100)	0 (0)	50 (96.2)
28 days post-vaccination	1 (2.4%) [0.1, 12.6]	6 (100) [54.1, 100.0]	248 (98.8) [96.5, 99.8]	52 (100) [93.2, 100.0]
6 months post-vaccination	0 (0%) [0.0, 9.0]	6 (100) [54.1, 100.0]	232 (99.1) [96.9, 99.9]	45 (97.8) [88.5, 99.9]

Abbreviations: CI=confidence interval; μPRNT$_{50}$=50% micro plaque reduction neutralization test; PP=per-protocol (population)

Antibody persistence

Persistence of the immune response was evaluated 12 and 24 months post-vaccination in VLA1553-303. All the participants were negative at baseline (pre-vaccination) for CHIKV-specific neutralizing antibodies. Proportion of participants with a CHIKV-specific neutralizing antibody response ≥150 μPRNT50 was 99.5% (183/184) and 97.1% (268/276), respectively at 1 and 2 year post-vaccination.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with IXCHIQ Vaccine in one or more subsets of the paediatric population in active immunisation for the prevention of disease caused by chikungunya virus (CHIKV) (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Not relevant to vaccines.

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.

A reproductive toxicity trial studying in female rats showed that IXCHIQ administered prior and after mating did not affect the reproductive parameters, the delivery, the foetal or pup development. There was evidence of placental and milk transfer of IXCHIQ-specific antibodies (see section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder

Sucrose
D-Sorbitol
L-Methionine
Trisodium Citrate Di-Hydrate
Magnesium Chloride
Di-Potassium- Hydrogen Phosphate

Potassium-Di- Hydrogen-Phosphate
recombinant Human Albumin (rHA) produced in yeast (Saccharomyces cerevisiae)

Solvent

Sterile water for injections

6.2 Incompatibilities

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

6.3 Shelf life

Unopened vial

2 years.
Do not freeze.

After reconstitution

In-use stability of the reconstituted vaccine has been demonstrated for 2 hours when stored either refrigerated at (2°C - 8°C) or at room temperature (15°C - 25°C). After this time, the reconstituted vaccine must be discarded.

From a microbiological point of view, after first opening 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

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

Stability data indicate that the vaccine components are stable for 24 hours in unopened vials when stored at temperatures from 23°C to 27°C. At the end of this period IXCHIQ should be used immediately or discarded. These data are intended to guide healthcare professionals in case of temporary temperature excursion only, it is not a recommended storage or shipping condition.

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

6.5 Nature and contents of container

IXCHIQ is supplied in a carton containing:

- One single-dose vial (type I glass) containing lyophilized powder of the vaccine with a rubber stopper (bromobutyl) and an aluminium flip-off cap with polypropylene closure.

- One solvent consisting of 0.5 mL sterile water for injection in a prefilled syringe with a rubber stopper (Flurotec®) and a tip cap (bromobutyl) (packaged without needles).

- Pack size: 1 vial of powder, 1 pre-filled syringe of solvent without needles.

6.6 Special precautions for disposal and other handling

Preparation for administration

The vaccine must be reconstituted only with the solvent provided prior to administration.

The reconstituted vaccine is a clear, colorless to slightly yellowish liquid solution. The vaccine should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If either of these conditions exists, do not administer the vaccine.

A needle (22-25G) with appropriate length of preferably at least 40 mm (1 1/2") should be used for reconstitution of the vaccine.

The syringe is for one-time use only.

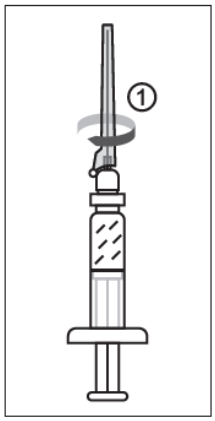

Figure 1

1) After removing the syringe cap, attach a needle on the luer lock of the syringe.

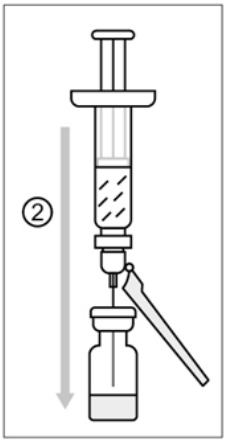

Figure 2

2) Cleanse the vial stopper. Slowly transfer the entire contents of the prefilled syringe (solvent) into the vial (powder).

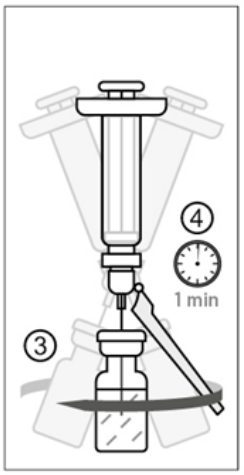

Figure 3

3) Gently swirl the vial to dissolve the powder. Do not shake or invert the vial.
4) After swirling, wait for at least one minute for complete reconstitution of the vaccine.

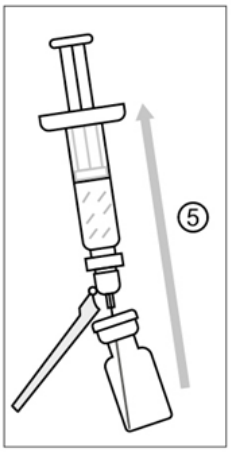

Figure 4

5) After reconstitution, slightly tilt the vial and withdraw the entire contents (0.5 mL) of the reconstituted vaccine into the same syringe. Do not invert the vial in order to ensure complete withdrawal of the reconstituted volume.

After reconstitution, administer IXCHIQ intramuscularly within 2 hours. If not used within 2 hours, discard the reconstituted vaccine (see section 6.3).

Disposal

This product contains genetically modified organisms (GMOs).

Any unused vaccine or waste material should be disposed of in accordance with local guidance for pharmaceutical waste. Potential spills should be cleaned up immediately and disinfected according to local policies. Dispose of the used syringe and needle in a sharps container such as a closeable, puncture resistant container.

7. MARKETING AUTHORISATION HOLDER

Valneva Austria GmbH
Campus Vienna Biocenter 3
1030 Vienna, Austria

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/24/1828/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28 June 2024

10. DATE OF REVISION OF THE TEXT

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 0TG
Scotland, UK

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

Valneva Austria GmbH
Campus Vienna Biocenter 3
1030 Vienna
Austria

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's 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.

- **Obligation to conduct post-authorisation measures**

The MAH shall complete, within the stated timeframe, the below measures:

Description	Due date
Post-authorisation efficacy study (PAES): In order to confirm the efficacy of IXCHIQ in individuals 12 years and older, the MAH should conduct, according to an agreed protocol, and submit the results of, a randomized, controlled trial with pragmatic elements to assess the effectiveness of IXCHIQ vaccination in the prevention of symptomatic, laboratory confirmed chikungunya after a single vaccination with IXCHIQ in adults in endemic areas.	Final report due date : 31 Dec 2029

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

IXCHIQ powder and solvent for solution for injection
Chikungunya vaccine (live)

2. STATEMENT OF ACTIVE SUBSTANCE(S)

After reconstitution, 1 dose (0.5 mL) contains Chikungunya virus Δ5nsP3 strain (live, attenuated), not less than 3.0 $\log_{10}$ $TCID_{50}$.

3. LIST OF EXCIPIENTS

Powder
Sucrose
D-Sorbitol
L-Methionine
Trisodium Citrate Di-Hydrate
Magnesium Chloride
Di-Potassium- Hydrogen Phosphate
Potassium-Di- Hydrogen-Phosphate
recombinant Human Albumin (rHA)

Solvent
Sterile water for injections

See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection.
1 vial of powder
1 prefilled syringe of solvent

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Reconstitute powder with solvent before administration.
Intramuscular use

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

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP
Discard reconstitued vaccine, if not used within 2 hours when kept refrigerated (2°C -8°C) or at room temperature (15°C - 25°C).

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Store in the outer carton to protect from light.
Do not freeze.

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

Dispose of in accordance with local guidance for pharmaceutical waste.

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/1/24/1828/001

13. BATCH NUMBER<, DONATION AND PRODUCT CODES>

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

LABEL FOR POWDER VIAL

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

IXCHIQ powder for solution for injection.
Chikungunya vaccine (live)
IM

2. METHOD OF ADMINISTRATION

Intramuscular use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 dose (0.5 mL) after reconstitution.

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL FOR PREFILLED SYRINGE

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

Solvent for IXCHIQ

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

0.5 mL

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

IXCHIQ powder and solvent for solution for injection
Chikungunya vaccine (live)

▼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 start receiving this medicine 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 IXCHIQ is and what it is used for

IXCHIQ is a vaccine that helps protect adults and adolescents aged between 12 and 64 years old against disease caused by the Chikungunya virus (CHIKV).

Chikungunya is a disease that is caused by the chikungunya virus (CHIKV), which is found in the sub-tropical regions of the Americas, Africa, Southeast Asia, India, and the Pacific Region. CHIKV is spread to humans by the bite of an infected mosquito. The majority of people infected with CHIKV develop a sudden fever and severe pain in multiple joints. Other symptoms may include headache, muscle pain, joint swelling, or rash. These symptoms typically resolve within 7 to 10 days, but symptoms may last for months or years.

Talk to your doctor, pharmacist or nurse first to decide if you should be given this vaccine.

How the vaccine works
IXCHIQ works by teaching the immune system (the body's natural defences) to defend itself against CHIKV. The vaccine contains a form of the virus that has been weakened in the laboratory so it can not multiply. When the body encounters this weakened version of the virus, the immune system will recognise it and produce antibodies to attack it. When a vaccinated person later comes into contact with the virus, their immune system will recognise it and be ready to defend the body against it. This helps protect them from getting sick.

2. What you need to know before you receive IXCHIQ

The vaccine must not be given:

- If you are allergic to the active substance or any of the other ingredients of this vaccine (listed in section 6).
- If your immune system has a reduced ability to fight infections and other diseases (immunodeficiency) or you have a weakened immune system (immunocompromised) because of a disease or a medicine (such as cancer and chemotherapy, inherited immune problems, long-term use of drugs that weaken the immune system such as corticosteroids or immunosuppressants, or HIV infection).
- If you are 65 years of age or older

Warnings and precautions
Talk to your doctor or, pharmacist or nurse before you receive IXCHIQ:
- If you have ever had a severe allergic reaction after any other vaccine injection.
- If you have anxiety related to needles or injections or if you have ever fainted following any injection.
- If you have a problem with bleeding or bruising, or if you are taking an anticoagulant medicine (to prevent blood clots).
- If you have a recent onset of fever (body temperature over 38°C). However, you can have your vaccination if you have a mild fever or upper airway infection like a cold.

Do not donate blood for at least 4 weeks after you have been vaccinated with IXCHIQ.

If you are not sure if any of the above applies to you, talk to your doctor, pharmacist or nurse before you are given the vaccine.

IXCHIQ may not fully protect everyone who gets the vaccine.
IXCHIQ does not protect against other diseases transmitted by mosquitoes.

You should still protect yourself from mosquito bites even after you have received the IXCHIQ vaccine. When traveling to countries with chikungunya virus, use insect repellent, wear long-sleeved shirts and pants and stay in places with air conditioning or that use window and door screens.

Children and adolescents
IXCHIQ can be used in adolescents aged 12 years and older. IXCHIQ has not been tested fully in young people under 12 years of age. It should not be used in this age group.

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

Pregnancy, breast-feeding and fertility
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 receiving this vaccine.

IXCHIQ has not been studied in pregnant women or nursing mothers.

Driving and using machines
Some of the side effects of IXCHIQ (see 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.

IXCHIQ contains sodium and potassium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.
This medicine contains potassium, less than 1 mmol (39 mg) per dose, i.e. essentially ‘potassium-free’.

3. How IXCHIQ is given

IXCHIQ is given as a single injection of 0.5 mL into the muscle of your upper arm by a doctor, pharmacist or nurse.

The dose for adolescents aged 12 to <18 years is the same as for adults.

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

4. Possible side effects

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

Get urgent medical attention if you get symptoms of a severe allergic reaction. Such reactions may include a combination of any of the following symptoms:

- difficulty breathing
- hoarseness or wheezing
- hives or rash
- swelling of your lips, face or throat
- dizziness
- weakness
- fast heartbeat

The following side effects may also occur after receiving this vaccine.

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

- headache
- feeling sick (nausea)
- tiredness (fatigue)
- muscle pain (myalgia)
- joint pain (arthralgia)
- fever
- tenderness, pain, redness (erythema), hardening (induration), or swelling where the injection is given
- low levels of white blood cells
- high levels of liver enzymes, as measured in blood tests

Common (may affect up to 1 in 10 people):

- swollen lymph nodes (lymphadenopathy)
- skin rash
- chills
- back pain
- dizziness
- diarrhoea
- vomiting
- eye pain

Uncommon (may affect up to 1 in 100 people):

- pins and needles, a burning or prickling sensation that is usually felt in the hands, arms, legs, or feet (paraesthesia)
- dilation and redness of the eyelid vessels

- ringing or buzzing in the ears (tinnitus),
- shortness of breath (dyspnoea)
- excessive sweating (hyperhidrosis)
- physical weakness (asthenia)
- swelling of lower legs or hands (peripheral oedema)

Rare (may affect up to 1 in 1 000 people):
- low amounts of water and sodium in the blood (hypovolaemic hyponatraemia).

Reporting of side effects
If you get any side effects, talk to your doctor or, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V.* By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store IXCHIQ

Keep this medicine out of the sight and reach of children.
Your doctor, pharmacist or nurse is responsible for storing this medicine and disposing of any unused product correctly. The following information is intended for healthcare professionals.

Do not use this medicine after the expiry date which is stated on the carton, vial and syringe after "EXP". The expiry date refers to the last day of that month.

Store in a refrigerator (2 °C to 8 °C). Do not freeze.
Store in the outer carton in order to protect from light.

In-use stability of the reconstituted vaccine has been demonstrated for 2 hours when stored either refrigerated at (2°C - 8°C) or at room temperature (15°C - 25°C). After this time, the reconstituted vaccine must be discarded.

From a microbiological point of view, after first opening the vaccine should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Do not throw away any vaccines via wastewater or household waste. Your doctor or nurse will dispose of this vaccine.These measures will help protect the environment.

6. Contents of the pack and other information

What IXCHIQ contains

After reconstitution, one dose (0.5 mL) contains Chikungunya virus Δ5nsP3 strain (live, attenuated)*, not less than 3.0 $\log_{10}$ $TCID_{50}$**.
* Produced in Vero cells
** 50% tissue culture infectious dose

This product contains genetically modified organisms (GMOs).

The other ingredients are:
Powder: Sucrose, D-Sorbitol, L-Methionine, Trisodium Citrate Di-Hydrate, Magnesium Chloride, Di-Potassium- Hydrogen Phosphate, Potassium-Di- Hydrogen-Phosphate and recombinant Human Albumin (rHA produced in yeast (Saccharomyces cerevisiae)).
Solvent: Sterile water for injections

See Section 2 “the vaccine contains sodium and potassium”.

What IXCHIQ looks like and contents of the pack

IXCHIQ is a powder and solvent for solution for injection. The powder is white to slightly yellowish. The solution is a clear colourless liquid.

Each pack of IXCHIQ contains:
- 1 vial containing the IXCHIQ component powder for 1 dose as a white to slightly yellowish powder.
- 1 pre-filled syringe containing the solvent for 1 dose sterile water component as a clear solution.

The contents of the two components (vial and syringe) are to be mixed prior to vaccination providing one dose of 0.5 mL.

Marketing Authorisation Holder and Manufacturer
Valneva Austria GmbH
Campus Vienna Biocenter 3
1030 Vienna
Austria
infoixchiq@valneva.com

This leaflet was last revised in

Other sources of information

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

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The following information is intended for healthcare professionals only:

The vaccine must be reconstituted only with the solvent provided prior to administration.

A needle (22-25G) with appropriate length of preferably at least 40 mm (1 1/2") should be used for reconstitution of the vaccine.

The syringe is for one-time use only.

The reconstituted vaccine is a clear, colorless to slightly yellowish liquid solution. The vaccine should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If either of these conditions exists, do not administer the vaccine.

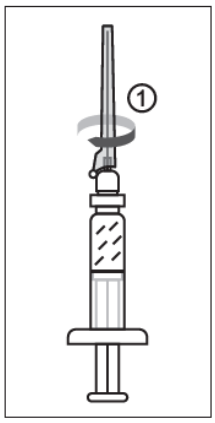

Figure 1

1) After removing the syringe cap, attach a needle on the luer lock of the syringe.

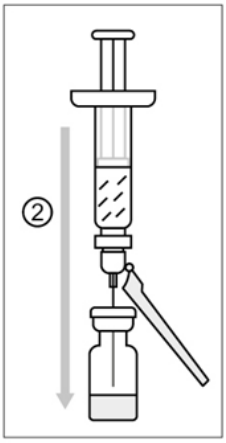

Figure 2

2) Cleanse the vial stopper. Slowly transfer the entire contents of the prefilled syringe (solvent) into the vial (powder).

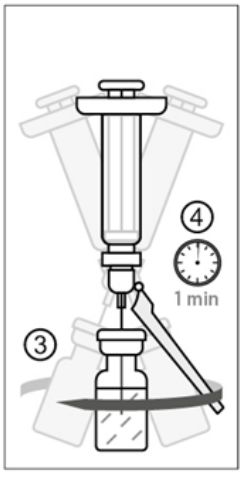

Figure 3

3) Gently swirl the vial to dissolve the powder. Do not shake or invert the vial.
4) After swirling, wait for at least one minute for complete reconstitution of the vaccine.

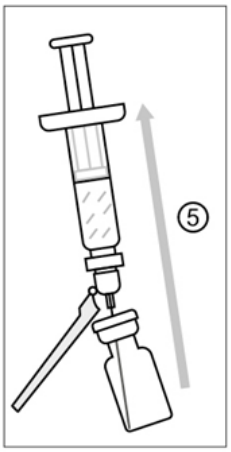

Figure 4

5) After reconstitution, slightly tilt the vial and withdraw the entire contents (0.5mL) of the reconstituted vaccine into the same syringe. Do not invert the vial in order to ensure complete withdrawal of the reconstituted volume.

After reconstitution, administer IXCHIQ intramuscularly within 2 hours. If not used within 2 hours, discard the reconstituted vaccine.

Disposal

This product contains genetically modified organisms (GMOs). Any unused vaccine or waste material should be disposed of in compliance with the local guidance for pharmaceutical waste. Potential spills should be cleaned up immediately and disinfected according to local policies. Dispose of the used syringe and needle in a sharps container such as a closeable, puncture resistant container