

## TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

# PRODUCT MONOGRAPH INCLUDING PATIENT MEDICATION INFORMATION

## IXCHIQ®

Chikungunya Vaccine, live, attenuated  
Powder for Solution for Intramuscular Injection  
Not less than 3.0 log<sub>10</sub> TCID<sub>50</sub>/0.5mL

Active immunizing agent

ATC code: J07BX07

Valneva Austria GmbH  
Campus Vienna Biocenter 3  
1030 Vienna  
Austria

Imported by:  
Quality & Compliance Services Inc.  
Mississauga  
ON L5N 1V8

Manufactured for:  
Valneva Canada Inc.  
Kirkland  
QC H9H 5B9

Submission Control Number: 299444

Date of Initial  
Authorization:  
June 20, 2024

Date of Revision:  
January 14, 2026

**RECENT MAJOR LABEL CHANGES**

<b>1</b>	<b>INDICATIONS</b>	<b>December 2025</b>
	1.1 Pediatrics	August 2025
<b>2</b>	<b>CONTRAINDICATIONS</b>	<b>December 2025</b>
<b>3</b>	<b>SERIOUS WARNINGS AND PRECAUTIONS BOX</b>	<b>December 2025</b>
<b>7</b>	<b>WARNINGS AND PRECAUTIONS</b>	<b>December 2025</b>
	7.1.3 Pediatrics	August 2025

**TABLE OF CONTENTS**

Sections or subsections that are not applicable at the time of authorization are not listed.

**RECENT MAJOR LABEL CHANGES** ..... 2

**TABLE OF CONTENTS** ..... 2

**PART I: HEALTH PROFESSIONAL INFORMATION** ..... 4

**1 INDICATIONS** ..... 4

    1.1 Pediatrics ..... 4

    1.2 Geriatrics ..... 4

**2 CONTRAINDICATIONS** ..... 5

**3 SERIOUS WARNINGS AND PRECAUTIONS BOX** ..... 6

**4 DOSAGE AND ADMINISTRATION** ..... 7

    4.1 Dosing Considerations ..... 7

    4.2 Recommended Dose and Dosage Adjustment ..... 7

    4.3 Reconstitution ..... 7

    4.4 Administration ..... 8

    4.5 Missed Dose ..... 8

**5 OVERDOSAGE** ..... 9

**6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING** ..... 10

**7 WARNINGS AND PRECAUTIONS** ..... 11

    7.1 Special Populations ..... 13

        7.1.1 Pregnant Women ..... 13

        7.1.2 Breast-feeding ..... 13

        7.1.3 Pediatrics ..... 13

        7.1.4 Geriatrics ..... 14

**8 ADVERSE REACTIONS** ..... 15

    8.1 Adverse Reaction Overview ..... 15

    8.2 Clinical Trial Adverse Reactions ..... 15

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

8.2.1 Clinical Trial Adverse Reactions – Pediatrics..... 23

8.3 Less Common Clinical Trial Adverse Reactions..... 23

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and  
Other Quantitative Data..... 24

8.5 Post-Market Adverse Reactions..... 25

**9 DRUG INTERACTIONS..... 27**

9.2 Drug Interactions Overview ..... 27

9.7 Drug-Laboratory Test Interactions ..... 27

**10 CLINICAL PHARMACOLOGY ..... 28**

10.1 Mechanism of Action ..... 28

10.2 Pharmacodynamics ..... 28

10.3 Pharmacokinetics..... 28

**11 STORAGE, STABILITY AND DISPOSAL..... 29**

**12 SPECIAL HANDLING INSTRUCTIONS ..... 30**

**PART II: SCIENTIFIC INFORMATION..... 31**

**13 PHARMACEUTICAL INFORMATION..... 31**

**14 CLINICAL TRIALS..... 32**

14.1 Trial Design and Study Demographics..... 32

14.2 Study Results ..... 34

**15 MICROBIOLOGY..... 38**

**16 NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY ..... 39**

**PATIENT MEDICATION INFORMATION ..... 41**

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND  
PRECAUTIONS BOX

DOSAGE AND  
ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS,  
COMPOSITION  
AND PACKAGING

WARNINGS  
AND PRECAUTIONS

ADVERSE  
REACTIONS

DRUG  
INTERACTIONS

CLINICAL  
PHARMACOLOGY

STORAGE, STABILITY  
AND DISPOSAL

SPECIAL HANDLING  
INSTRUCTIONS

PHARMACEUTICAL  
INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL  
TOXICOLOGY AND  
PHARMACOLOGY

PATIENT MEDICATION  
INFORMATION

## **PART I: HEALTH PROFESSIONAL INFORMATION**

### **1 INDICATIONS**

IXCHIQ (chikungunya vaccine, live, attenuated) Powder for Solution for Intramuscular Injection is a live-attenuated vaccine, intended for active immunization in individuals 12 years and older for the prevention of disease caused by the chikungunya virus (CHIKV), as a single-dose immunization.

Please refer to the Committee to Advise on Tropical Medicine and Travel (CATMAT) for guidance on the use of the travel-related vaccines in Canada, including IXCHIQ.

#### **1.1 Pediatrics**

The safety and immunogenicity of IXCHIQ have not been established in individuals under 12 years of age. Therefore, Health Canada has not authorized an indication for individuals under 12 years of age.

#### **1.2 Geriatrics**

Clinical studies of IXCHIQ include participants 65 years of age and older and their data contribute to the overall assessment of safety and immunogenicity.

## 2 CONTRAINDICATIONS

IXCHIQ is contraindicated in:

- Individuals with current or suspected immunodeficiency or immunosuppression (e.g., from malignancies such as hematologic cancers and solid tumors, recent chemotherapy, congenital immunodeficiency, long-term immunosuppressive therapy for chronic conditions such as autoimmune disorders or organ transplants, or poorly managed HIV infection with immunocompromised state).
- Patients who are hypersensitive to this vaccine or to any ingredient in the formulation or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.
- Pregnancy. Women of child-bearing potential should be advised to avoid pregnancy for one month following vaccination (see also 7 WARNINGS AND PRECAUTIONS).

### TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS 

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

### 3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Available post-marketing data suggest that individuals 65 years of age and older who are medically frail with multiple chronic medical conditions may have an increased risk for serious and life-threatening adverse reactions following recent vaccination with IXCHIQ.

#### TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

## 4 DOSAGE AND ADMINISTRATION

### 4.1 Dosing Considerations

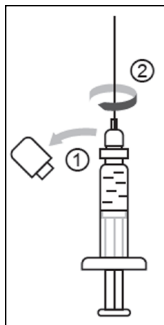
For intramuscular injection only.

### 4.2 Recommended Dose and Dosage Adjustment

One single dose of IXCHIQ, which is 0.5 mL after reconstitution.

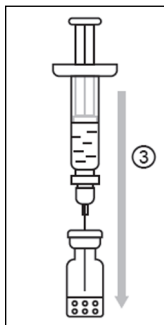
### 4.3 Reconstitution

Reconstitute the Lyophilized IXCHIQ Powder only with the accompanying Sterile Water Diluent. 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 reconstituted vaccine is a clear, colorless to slightly yellowish liquid solution [See 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING]. The reconstituted vaccine should be inspected visually for particulate matter and discoloration prior to administration. If either of these conditions exists, do not administer the vaccine. Follow the figure descriptions below for preparation.



**Figure 1**

- 1) Remove the cap from the syringe of Sterile Water Diluent.
- 2) Attach a needle to the Luer lock of the syringe.



**Figure 2**

- 3) Cleanse the stopper of the vial of Lyophilized Powder. Slowly transfer the entire content of the prefilled syringe of diluent into the vial containing lyophilized powder.

## TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

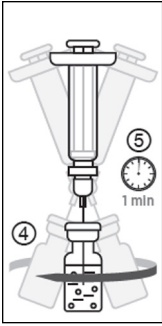
PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

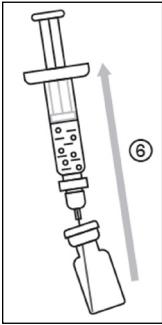
NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION



**Figure 3**

- 4) Gently swirl the vial to dissolve the lyophilized IXCHIQ. Avoid strong shaking or inverting of the vial.
- 5) Wait for at least one minute for complete reconstitution of the vaccine.



**Figure 4**

- 6) After reconstitution, slightly tilt the vial to withdraw the entire contents of the reconstituted IXCHIQ into the same syringe. Avoid inverting the vial.

Changing needles between withdrawing the vaccine from the vial and injecting it into a recipient is not necessary unless the needle has been damaged or contaminated.

Dispose of used sharps and needles according to your local requirements.

#### 4.4 Administration

Administer the reconstituted IXCHIQ vaccine intramuscularly (i.m.) into the deltoid muscle immediately. If not used immediately, store the reconstituted vaccine at room temperature and administer within 30 minutes.

Discard vaccine if not used within 30 minutes.

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

Immunity following Chikungunya virus infection is thought to convey lifelong immunity. The need for a booster dose following immunization with the live-attenuated vaccine has not been established.

#### 4.5 Missed Dose

Not applicable.

## TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

## 5 OVERDOSAGE

No case of overdose has been reported with IXCHIQ. In the event of overdose, monitoring of vital functions and possible symptomatic treatment is recommended.

For management of a suspected drug overdose, contact your regional poison control centre.

### TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE



DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

## 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of vaccines for patient immunization record-keeping as well as safety monitoring, health professionals should record the time and date of administration, quantity of administered dose (if applicable), anatomical site and route of administration, brand name and generic name of the vaccine, the product lot number and expiry date.

**Table 1: Dosage Forms, Strengths, Composition and Packaging**

Route of Administration	Dosage Form / Strength / Composition	Non-medicinal Ingredients
Intramuscular	Powder for Solution for Injection/  Each 0.5 mL dose of the vaccine contains not less than 3.0 log <sub>10</sub> TCID <sub>50</sub> of live attenuated chikungunya virus.	D-Sorbitol (0.5% (w/w)), L-Methionine (10 mM), Magnesium Chloride (5 mM), Potassium Phosphate (5 mM), Recombinant Human Albumin (rHA) (0.01%), Sucrose (5% (w/w)), Trisodium citrate di-hydrate (25 mM)

IXCHIQ is supplied as a single-dose vial of lyophilized powder to be reconstituted with the supplied prefilled syringe of diluent (sterile water for injection). A single dose is 0.5 mL after reconstitution. Each 0.5 mL dose of the vaccine contains not less than 3.0 log<sub>10</sub> TCID<sub>50</sub> of live attenuated chikungunya virus.

The appearance of the lyophilized vaccine prior to reconstitution is white to slightly yellowish homogeneous powder. After reconstitution, the solution is a clear, colorless to slightly yellow.


INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING 

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

## 7 WARNINGS AND PRECAUTIONS

### General

IXCHIQ should only be given when there is a significant risk of acquiring chikungunya infection, and after careful consideration of the potential risks and benefits (see 8 ADVERSE REACTIONS and 14 CLINICAL TRIALS).

During post-marketing use, serious adverse reactions following vaccination with IXCHIQ were most commonly reported in medically frail individuals with advanced chronic diseases, individuals at older age (i.e.,  $\geq 65$  years of age, especially  $\geq 75$  years of age), and those with a high risk of having an undiagnosed immunocompromised condition (e.g., occult cancer or immunosenescence).

Severe reactogenicity or chikungunya-like adverse reactions in medically frail individuals with chronic diseases may lead to deterioration of general condition including malaise and decreased appetite, exacerbation of preexisting diseases, confusional state, encephalopathy, or encephalitis, leading to falls, hospitalisation and death. Vaccinees should be instructed to promptly seek medical attention if they experience, after vaccination, symptoms suggestive of severe reactogenicity or severe chikungunya-like adverse reactions.

As with other vaccines, vaccination with IXCHIQ should be postponed in individuals suffering from an acute severe febrile illness or infection.

Syncope (fainting) can occur following, or even before, any vaccination as a vasovagal response to the needle injection, in the context of an anxiety-related reaction. It is important that procedures are in place to avoid injury from fainting.

Vaccination with IXCHIQ may not protect all individuals. It is recommended to continue personal protection measures against mosquito bites after vaccination.

### Acute Allergic Reactions

Appropriate medical treatment and supervision must be available to manage immediate allergic reactions in the event an acute anaphylactic reaction occurs following administration of IXCHIQ.

### Driving and Operating Machinery

No studies on the effects of IXCHIQ on the ability to drive and use machines have been performed. However, some of the effects (e.g., severe systemic reactogenicity) mentioned under 8 ADVERSE REACTIONS may temporarily affect the ability to drive or use machines. Exercise caution when driving or operating a vehicle or potentially dangerous machinery.

### Hematologic

As with other vaccines administered intramuscularly, IXCHIQ should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following an intramuscular administration to these individuals.

### Musculoskeletal

#### • Immune-mediated Arthritis

Available data in adults and adolescents with a history of immune-mediated or clinically relevant arthritis are not sufficient to determine the safety of IXCHIQ, as this condition was an exclusion criterion for participation in clinical trials.

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS 

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

• **Chikungunya-like Prolonged Arthralgia**

During post-marketing, additional cases of prolonged chikungunya-like arthralgia occurred after vaccination with IXCHIQ with a range of duration from a few weeks to more than 5 months with a few cases requiring follow-up with rheumatology. Vaccinees should be instructed to promptly seek medical attention if experiencing, after vaccination, symptoms suggestive of prolonged arthralgia.

**Neurologic**

• **Encephalitis and encephalopathy**

Encephalitis and encephalopathy (including with fatal outcome) have been reported during post-marketing use of IXCHIQ in individuals 74 years and older with multiple comorbidities. Vaccinees should be instructed to promptly seek medical attention if they experience, after vaccination, signs or symptoms suggestive of a neurological disorder.

**Reproductive Health: Female and Male Potential**

• **Fertility**

Reproductive and developmental toxicology of IXCHIQ was conducted in a single pre- and post-natal developmental toxicity study in pregnant rats which did not identify significant adverse effects in female fertility (See 16. NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY section). No studies in male fertility were conducted.

• **Teratogenic Risk**

Reproductive and developmental toxicology of IXCHIQ was conducted in a single pre- and post-natal developmental toxicity study in pregnant rats which did not identify significant adverse effects in fetal examination (See 16. NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY section).

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND  
PRECAUTIONS BOX

DOSAGE AND  
ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS,  
COMPOSITION  
AND PACKAGING

WARNINGS  
AND PRECAUTIONS



ADVERSE  
REACTIONS

DRUG  
INTERACTIONS

CLINICAL  
PHARMACOLOGY

STORAGE, STABILITY  
AND DISPOSAL

SPECIAL HANDLING  
INSTRUCTIONS

PHARMACEUTICAL  
INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL  
TOXICOLOGY AND  
PHARMACOLOGY

PATIENT MEDICATION  
INFORMATION

**7.1 Special Populations**

**7.1.1 Pregnant Women**

Women of child-bearing potential should be advised to avoid pregnancy for one month following vaccination. Available data in pregnant women are not sufficient to determine the safety of IXCHIQ regarding pregnancy, embryofetal development, parturition and postnatal development.

No adequate and well-controlled studies of IXCHIQ have been performed among pregnant women. Human data available from clinical trials with IXCHIQ are insufficient to establish the presence or absence of vaccine-associated risk during pregnancy. One developmental toxicity study was performed in female rats, see 16 NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY section).

Disease-associated maternal and/or embryo/fetal risk

Vertical transmission of CHIKV from mothers with viremia at delivery to their infants has been reported and can cause severe, potentially fatal neurological disease in neonates.

Fetal/neonatal adverse reactions

Vaccine viremia can occur 3 to 7 days after vaccination and is resolved by 14 days after vaccination [See 10.3 Pharmacokinetics]. The potential for transmission of the vaccine virus from mother to infant is unknown.

Pregnancy Exposure

Women who received IXCHIQ during pregnancy are encouraged to report any suspected exposure or adverse reactions to Valneva Canada, or ask their healthcare professional to do so, at 1-855-356-0831

**7.1.2 Breast-feeding**

It is unknown if IXCHIQ is excreted in human milk. Precaution should be exercised because many drugs can be excreted in human milk.

One developmental toxicity study performed in rats showed IXCHIQ-specific antibodies in the milk of vaccinated female rats from day 5 of lactation.

Human data are not available to assess the impact of IXCHIQ on milk production, its presence in breast milk, or its effects on the breastfed child. Vaccine viremia can occur 3 to 14 days after vaccination and is resolved by 14 days after vaccination [See 10.3 Pharmacokinetics]. The potential for transmission of the vaccine virus from mother to infant through breastmilk is unknown. To date, no infants have been found to be infected with CHIKV or vaccine virus through breastfeeding. 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 or from the underlying maternal condition.

**7.1.3 Pediatrics**

The safety and immunogenicity of IXCHIQ in children under 12 years of age have not yet been established. Therefore, Health Canada has not authorized the use of IXCHIQ under 12 years of age.

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS 

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

### 7.1.4 Geriatrics

Clinical studies of IXCHIQ include participants 65 years of age and older and their data contribute to the overall assessment of safety and immunogenicity (see 8 ADVERSE REACTIONS and 14 CLINICAL).

Available post-marketing data suggest that individuals 65 years of age and older who are medically frail with multiple chronic medical conditions may have an increased risk for *serious and life-threatening adverse reactions* following recent vaccination with IXCHIQ. During post-marketing use with IXCHIQ, serious chikungunya-like illness resulting in hospitalizations and one death has been reported [see 8.5 Post-marketing Adverse Reactions]. The decision to vaccinate individuals 65 years of age and older needs to weigh the risks and benefits of vaccination.

## TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS



ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS



DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

## 8 ADVERSE REACTIONS

### 8.1 Adverse Reaction Overview

#### Adults

In clinical study VLA1553-301, the most common solicited injection site reaction in adults was tenderness (10.6%). The most common solicited systemic adverse reactions in the first 10 days after vaccination were headache (31.6%), fatigue (28.5%), and myalgia/muscle pain (23.9%), arthralgia (17.2%), and fever (13.5%).

#### Adolescents 12 to <18 years of age

##### *Chikungunya virus baseline seronegative adolescents*

In clinical study VLA1553-321, the most common solicited injection site reactions in adolescents who received IXCHIQ and were baseline seronegative for prior exposure to CHIKV were tenderness (21.6%) and pain (18.6%). The most common solicited systemic adverse reactions in the first 10 days after vaccination were headache (54.7%), myalgia (28.7%), fever (28.2%), fatigue (24.8%), nausea (17.4%), and arthralgia (14.5%).

##### *Chikungunya virus baseline seropositive adolescents*

The proportion of participants that experienced solicited systemic AEs was lower in baseline seropositive participants vaccinated with IXCHIQ than in baseline seronegative participants vaccinated with IXCHIQ (44.7% and 67.9%, respectively). The most common solicited systemic adverse reactions in baseline seropositive IXCHIQ recipients within the first 10 days after vaccination were headache (35.1%), myalgia (19.1%), fatigue (11.7%), nausea (9.6%), arthralgia (6.4%) and fever (6.4%). The proportion of participants who experienced solicited local AEs and unsolicited AEs was similar in the IXCHIQ arms regardless of baseline serostatus.

### 8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials, therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

#### Adults ≥18 years of age

The safety profile of IXCHIQ was evaluated from data generated from 3 randomized, multicenter clinical studies (VLA1553-301, VLA1553-302, and VLA1553-101) all conducted in North America in healthy adult participants 18 years of age and older. Study VLA1553-101 was done using an earlier formulation and was a supportive dose-escalation Phase I trial of IXCHIQ in 120 participants. Study VLA1553-301 was the pivotal double-blind placebo-controlled Phase III trial in 4,115 participants who received IXCHIQ or placebo (phosphate buffered saline or PBS) as a single dose (see 14 CLINICAL TRIALS). Study VLA1553-302 was a supportive non-placebo-controlled Phase III trial investigating the consistency of three lots of IXCHIQ given as a single dose in 408 participants.

The IXCHIQ safety data described herein were collected in 4,115 participants from the main VLA1553-301 clinical trial, randomized 3:1 to receive IXCHIQ or PBS (placebo). A total of 3,082 healthy adults 18 through 88 years of age received a single intramuscular dose ( $1 \times 10^4$  TCID<sub>50</sub>) of IXCHIQ and 1,033 received placebo. Participants were followed-up for safety for 6 months post-vaccination. Overall, 54.7% of participants were female. Ethnicity was reported as 80.4% White, 13.9% Black or African American, 1.7% Asian, 0.8% American Indian/Alaska Native, 0.4% Native Hawaiian/Pacific Islander and 2.8% as other. The IXCHIQ and placebo groups were similar with regard to demographics.

Adolescents 12 to <18 years of age

The safety of IXCHIQ in adolescents aged 12 to <18 years was evaluated in a Phase III clinical trial (VLA1553-321) conducted in Brazil. This randomized, double-blind, placebo-controlled trial enrolled 754 participants who received either a single intramuscular dose ( $1 \times 10^4$  TCID<sub>50</sub>) of IXCHIQ (n=502) or placebo (PBS; n=252), with a follow-up period of 6 months (see 14 CLINICAL TRIALS). At study entry, 18.4% of participants had pre-existing antibodies against CHIKV, while 81.4% were CHIKV-naïve. Randomization was stratified by CHIKV baseline serostatus.

In Study VLA1553-301 and Study VLA1553-321, solicited injection site adverse reactions (ARs) and eight solicited systemic ARs (fever, nausea, vomiting, headache, fatigue, myalgia, arthralgia and rash) were reported in 10 consecutive days after vaccination. Unsolicited ARs were captured in the entire post-vaccination period, i.e. up to Day 180 and Day 365 (after Day 180, only adverse events of special interest and serious adverse events were collected, and this was done in a subset of participants [n=348]) after vaccination in Study VLA1553-301 and Study VLA1553-321, respectively.

**Solicited Adverse Reactions**


Adults ≥18 years of age

Overall, 1,553/3,082 (50.4%) of IXCHIQ recipients vs 279/1,033 (27.0%) of placebo recipients experienced at least one solicited systemic adverse reaction (Table 2). The most common systemic adverse reactions of IXCHIQ recipients were headache (31.6%), fatigue (28.5%), myalgia (23.9%), arthralgia (17.2%), and fever (13.5%) of these most (>95%) were mild to moderate. Overall, 463/3,082 (15.0%) of IXCHIQ recipients vs 115 (11.1%) of placebo recipients experienced at least one injection site adverse reaction. The most common injection site adverse reaction (>10%) was tenderness (10.6%). The median day of onset was Day 2 after vaccination for local injection site adverse reactions (Day 1 was the day of vaccination). For systemic adverse reactions, the median onset was Day 5 after vaccination, which is two days after the observed peak in viremia on Day 3 after vaccination with IXCHIQ in adults in the phase I study (Study VLA1553-101) (see 10.3 Pharmacokinetics). Local and systemic adverse reactions resolved with a median duration of 2 days.

Adolescents 12 to <18 years of age

*Chikungunya virus baseline seronegative adolescents*

A total of 277/408 (67.9%) of baseline seronegative IXCHIQ recipients reported at least one solicited systemic adverse reaction, compared to 91/206 (44.2%) of baseline seronegative placebo recipients (Table 2). The most common solicited systemic adverse reactions among baseline seronegative IXCHIQ recipients were headache (54.7%), myalgia (28.7%), fever (28.2%), fatigue (24.8%), nausea (17.4%) and arthralgia (14.5%).

- INDICATIONS
- CONTRAINDICATIONS
- SERIOUS WARNINGS AND PRECAUTIONS BOX
- DOSAGE AND ADMINISTRATION
- OVERDOSAGE
- DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING
- WARNINGS AND PRECAUTIONS
- ADVERSE REACTIONS 
- DRUG INTERACTIONS
- CLINICAL PHARMACOLOGY
- STORAGE, STABILITY AND DISPOSAL
- SPECIAL HANDLING INSTRUCTIONS
- PHARMACEUTICAL INFORMATION
- CLINICAL TRIALS
- MICROBIOLOGY
- NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY
- PATIENT MEDICATION INFORMATION

The majority of solicited systemic adverse reactions (>94%) were of mild to moderate intensity.

175/408 (42.9%) of the baseline seronegative IXCHIQ recipients used analgesics and 31/408 (7.6%) used anti-inflammatory and antirheumatic products during the 10 days after vaccination. Of the baseline seronegative placebo recipients, 36/206 (17.5%) used analgesics and 9/206 (4.4%) used anti-inflammatory and antirheumatic products during the 10 days after vaccination.

One IXCHIQ recipient (0.2%) reported mild solicited arthralgia 7 days post-vaccination which lasted 13 days and resolved. During the same period, the individual also concomitantly experienced influenza, headache, myalgia, and eye pain and received analgesics and non-steroidal anti-inflammatory medications concomitantly to control symptoms.


Injection site adverse reactions were reported in 132/408 (32.4%) of baseline seronegative IXCHIQ recipients and 54/206 (26.2%) of baseline seronegative placebo recipients. The most common injection site reactions in baseline seronegative IXCHIQ recipients were tenderness (21.6%) and pain (18.6%). Solicited systemic and local adverse reactions resolved with a median duration of 1 to 2 days, depending on the type of adverse reaction.

*Chikungunya virus baseline seropositive adolescents*

The proportion of participants that experienced solicited systemic adverse reactions was lower in baseline seropositive participants vaccinated with IXCHIQ than in baseline seronegative participants vaccinated with IXCHIQ (42/94 participants [44.7%] and 277/408 participants [67.9%], respectively, see Table 2). The most common solicited systemic adverse reactions among baseline seropositive IXCHIQ recipients were headache (35.1%), myalgia (19.1%), fatigue (11.7%), nausea (9.6%), arthralgia (6.4%) and fever (6.4%). The majority of solicited systemic adverse reactions (>97%) were of mild to moderate intensity. 17/94 (18.1%) of the baseline seropositive IXCHIQ recipients used analgesics and 1/94 (1.1%) used anti-inflammatory and antirheumatic products during the 10 days after vaccination. Of the baseline seropositive placebo recipients, 3/45 (6.7%) used analgesics and none used anti-inflammatory and antirheumatic products during the 10 days after vaccination.

One (1.1%) baseline seropositive IXCHIQ recipient reported recurrence of arthralgia. The first episode started on Day 3 after vaccination, lasted 32 days, was mild in severity, and resolved. Other AEs around the time of arthralgia onset included solicited headache (Day 1-9), solicited nausea (Day 2-8), and unsolicited, unrelated pruritus (Day 3-18). No fever was documented in this participant. The second unsolicited arthralgia event started on Day 148 after vaccination and lasted 247 days. The event was assessed as unrelated to IXCHIQ vaccination. Despite the longer duration of this unsolicited arthralgia, this event is not considered chronic as it did not originate during the acute phase nor showed a continuous progression from acute to chronic symptoms (as observed with wild-type CHIKV infection).


The proportion of participants who experienced solicited injection site reactions was similar across both baseline serostatus groups in the IXCHIQ arm, with 29.8% in baseline seropositive participants and 32.4% in baseline seronegative participants.

- INDICATIONS
- CONTRAINDICATIONS
- SERIOUS WARNINGS AND PRECAUTIONS BOX
- DOSAGE AND ADMINISTRATION
- OVERDOSAGE
- DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING
- WARNINGS AND PRECAUTIONS
- ADVERSE REACTIONS 
- DRUG INTERACTIONS
- CLINICAL PHARMACOLOGY
- STORAGE, STABILITY AND DISPOSAL
- SPECIAL HANDLING INSTRUCTIONS
- PHARMACEUTICAL INFORMATION
- CLINICAL TRIALS
- MICROBIOLOGY
- NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY
- PATIENT MEDICATION INFORMATION

**Table 2: Solicited Systemic and Injection Site Adverse Reactions Within 10 Days After a Single Vaccination (Safety Population in Baseline Seronegative Adults in the Study VLA1553-301 and in Baseline Seronegative Adolescents and Baseline Seropositive Adolescents in the Study VLA1553-321)**

Adverse Reaction Category	Study VLA1553-301		Study VLA1553-321 Baseline Seronegative		Study VLA1553-321 Baseline Seropositive	
	IXCHIQ (N=3,082) n (%)	Placebo (PBS) (N=1,033) n (%)	IXCHIQ (N=408) n (%)	Placebo (PBS) (N=206) n (%)	IXCHIQ (N=94) n (%)	Placebo (PBS) (N=45) n (%)
<b>Any Solicited Adverse Reactions</b>	<b>1634 (53.0)</b>	<b>332 (32.1)</b>	<b>303 (74.3)</b>	<b>105 (51.0)</b>	<b>50 (53.2)</b>	<b>17 (37.8)</b>
<b>Solicited Systemic Adverse Reactions</b>	<b>1,553 (50.4)</b>	<b>279 (27.0)</b>	<b>277 (67.9)</b>	<b>91 (44.2)</b>	<b>42 (44.7)</b>	<b>15 (33.3)</b>
Headache	973 (31.6)	152 (14.7)	223 (54.7)	76 (36.9)	33 (35.1)	10 (22.2)
Fatigue	879 (28.5)	131 (12.7)	101 (24.8)	19 (9.2)	11 (11.7)	5 (11.1)
Myalgia/Muscle Pain	737 (23.9)	76 (7.4)	117 (28.7)	27 (13.1)	18 (19.1)	3 (6.7)
Arthralgia/Joint Pain	529 (17.2)	51 (4.9)	59 (14.5)	11 (5.3)	6 (6.4)	2 (4.4)
Fever ( $\geq 38^{\circ}\text{C}$ adults, $\geq 37.8^{\circ}\text{C}$ adolescents)	415 (13.5)	9 (0.9)	115 (28.2)	5 (2.4)	6 (6.4)	4 (8.9)
Nausea	345 (11.2)	58 (5.6)	71 (17.4)	29 (14.1)	9 (9.6)	2 (4.4)
Rash	70 (2.3)	5 (0.5)	17 (4.2)	1 (0.5)	1 (1.1)	1 (2.2)
Vomiting	59 (1.9)	10 (1.0)	12 (2.9)	9 (4.4)	1 (1.1)	0
<b>Solicited Injection Site Adverse Reactions</b>	<b>463 (15.0)</b>	<b>115 (11.1)</b>	<b>132 (32.4)</b>	<b>54 (26.2)</b>	<b>28 (29.8)</b>	<b>7 (15.6)</b>
Tenderness	328 (10.6)	84 (8.1)	88 (21.6)	33 (16.0)	12 (12.8)	3 (6.7)
Pain	191 (6.2)	38 (3.7)	76 (18.6)	29 (14.1)	21 (22.3)	4 (8.9)
Erythema/Redness	46 (1.5)	15 (1.5)	10 (2.5)	3 (1.5)	1 (1.1)	0
Induration	44 (1.4)	8 (0.8)	17 (4.2)	9 (4.4)	4 (4.3)	2 (4.4)
Swelling	21 (0.7)	8 (0.8)	7 (1.7)	7 (3.4)	0	0

All solicited injection site adverse reactions were graded as mild or moderate in severity, except for a single solicited injection site adverse reaction of pain (adult study), induration (one baseline seronegative adolescent), and erythema/redness (one baseline seronegative adolescent) graded as severe in the IXCHIQ group (See Section Serious Adverse Events for details).

- INDICATIONS
- CONTRAINDICATIONS
- SERIOUS WARNINGS AND PRECAUTIONS BOX
- DOSAGE AND ADMINISTRATION
- OVERDOSAGE
- DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING
- WARNINGS AND PRECAUTIONS
- ADVERSE REACTIONS** 
- DRUG INTERACTIONS
- CLINICAL PHARMACOLOGY
- STORAGE, STABILITY AND DISPOSAL
- SPECIAL HANDLING INSTRUCTIONS
- PHARMACEUTICAL INFORMATION
- CLINICAL TRIALS
- MICROBIOLOGY
- NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY
- PATIENT MEDICATION INFORMATION

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS



DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

Chikungunya-Like Adverse Reactions

Chikungunya-like adverse reactions (i.e. a cluster of symptoms consistent with typical symptoms of wild-type chikungunya infection), were defined by protocol as fever ( $\geq 38^\circ\text{C}$  in Study VLA1553-301 or  $\geq 37.8^\circ\text{C}$  in Study VLA1553-321) and one or more of any of the following: arthralgia or arthritis, myalgia, headache, back pain (only in Study VLA1553-301), rash or certain skin symptoms, lymphadenopathy (only in Study VLA1553-301), or certain neurological, cardiac (only in Study VLA1553-301) or ocular symptoms that occurred with an onset within 30 days after vaccination, regardless of whether they occurred simultaneously or not. Severe chikungunya-like adverse reactions included symptoms that prevented daily activity and/or required medical intervention.

Adults  $\geq 18$  years of age

In Study VLA1553-301, the occurrence of chikungunya-like adverse reactions was evaluated in a post-hoc analysis where 361 (11.7%) in the IXCHIQ group (n=3,082) reported chikungunya-like adverse reactions, including 48 participants (1.6%) who reported severe chikungunya-like adverse reactions. Six (0.6%) participants in the placebo group (n=1,033) reported chikungunya-like adverse reactions, none of which was severe.

The median onset of chikungunya-like adverse reactions in IXCHIQ recipients was 3 days (range 0 to 10 days) after vaccination. The median duration of chikungunya-like reactions in IXCHIQ recipients was 4 days (range 1 day to at least 6 months).

Twenty-two IXCHIQ recipients had prolonged chikungunya-like adverse reactions lasting longer than 14 days (median duration 33 days, range 15 days to at least 6 months) and 15 IXCHIQ recipients had chikungunya-like adverse reactions lasting longer than 28 days (median duration 94 days, range 29 days to at least 6 months).

Prolonged fatigue, myalgia, or headache (lasting longer than 14 days) were reported by 13 participants (nine of these participants had symptoms lasting longer than 28 days).

Prolonged arthralgia (lasting longer than 14 days) was reported by seven participants (five of these participants had arthralgia lasting longer than 28 days), including a 46-year-old male who reported severe arthralgia and back pain that lasted for at least 51 days after vaccination and a 50-year-old female who reported polyarthralgia and nodular swelling of joints in fingers and foot that lasted for at least 6 months after vaccination.

Additionally, a 62-year-old female with no recorded fever developed intermittent polyarthritis involving fingers for more than 8 months, including development of a trigger finger requiring surgical release 4-5 months after vaccination.

Adolescents 12 to <18 years of age

*Chikungunya virus baseline seronegative adolescents*

Among baseline seronegative participants, 110 participants (27.0%) in the IXCHIQ group (n=408) reported chikungunya-like adverse reactions, including 17 participants (4.2%) who reported severe chikungunya-like adverse reactions. Eight (3.9%) baseline seronegative participants in the placebo group (n=206) reported chikungunya-like adverse reactions, none thereof was severe.

15 IXCHIQ recipients (3.7%) and 3 placebo recipients (1.5%) had prolonged chikungunya-like adverse reactions lasting longer than 14 days (median duration 23 days, range 16 to 30 days).

Prolonged headache (lasting longer than 14 days) was reported in 2 baseline seronegative adolescents (23 days with moderate intensity and 29 days with mild intensity, respectively). There was one prolonged chikungunya-like symptom lasting 28 days or longer reported (mild headache lasting 29 days) in a IXCHIQ recipient.

*Chikungunya virus baseline seropositive adolescents*

The proportion of participants that experienced chikungunya-like adverse reactions was lower in baseline seropositive participants than in baseline seronegative participants vaccinated with IXCHIQ (6/94 participants [6.4%] and 110/408 participants [27.0%], respectively). One (1.1%) baseline seropositive IXCHIQ recipient reported a severe chikungunya-like adverse reaction. Four (8.9%) baseline seropositive participants in the placebo group reported chikungunya-like adverse reactions, one (2.2%) thereof was severe.

Two baseline seropositive participants (1 IXCHIQ recipient and 1 placebo recipient) had prolonged chikungunya-like adverse reactions lasting longer than 14 days (15 and 19 days, respectively).

No chikungunya-like symptoms lasting longer than 14 days were reported among baseline seropositive participants.

The frequencies of symptoms among the adult and adolescent IXCHIQ recipients with chikungunya-like adverse reactions are presented in Table 3.

**Table 3. Frequency of Symptoms Among Participants With Chikungunya-Like Adverse Reactions (in the Adults in Study VLA1553-301 and in the Baseline Seronegative Adolescents in Study VLA1553-321)**

Chikungunya-Like Symptom	Study VLA1553-301	Study VLA1553-321
	IXCHIQ (N=361) n (%)	IXCHIQ (N=110) n (%)
Pyrexia (any)	361 (100)	110 (100)
Headache (any)	280 (77.6)	96 (87.3)
Fatigue (any)	264 (73.1)	51 (46.4)
Myalgia (any)	215 (59.6)	62 (56.4)
Arthralgia (any)	159 (44.0)	33 (30.0)
Chills (any)	29 (8.0)	4 (3.6)
Rash (any)	22 (6.1)	11 (10.0)
Back pain (any)	13 (3.6)	Not reported
Lymphadenopathy (any)	9 (2.5)	Not reported
Dizziness (any)	6 (1.7)	Not reported
Pain (any)	4 (1.1)	Not reported
Paresthesia (any)	3 (0.8)	1 (0.9)
Hyperhidrosis (any)	2 (0.6)	Not reported
Edema peripheral (any)	2 (0.6)	Not reported
Asthenia (any)	1 (0.3)	Not reported
Ataxia (any)	1 (0.3)	Not reported

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS



DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

<b>Chikungunya-Like Symptom</b>	<b>Study VLA1553-301</b>	<b>Study VLA1553-321</b>
	<b>IXCHIQ (N=361) n (%)</b>	<b>IXCHIQ (N=110) n (%)</b>
Atrial fibrillation (any)	1 (0.3)	Not reported
Feeling abnormal (any)	1 (0.3)	Not reported
Hypoesthesia (any)	1 (0.3)	Not reported
Influenza like illness (any)	1 (0.3)	Not reported
Neuropathy peripheral (any)	1 (0.3)	Not reported
Rash erythematous (any)	1 (0.3)	Not reported
Syncope (any)	1 (0.3)	Not reported
Hand dermatitis (any)	Not reported	1 (0.9)
Rash maculo-papular (any)	Not reported	1 (0.9)

N=number of participants with chikungunya-like adverse reactions; n=number of participants with chikungunya-like symptom.

## Unsolicited Adverse Events

### Adults ≥18 years of age


In Study VLA1553-301, unsolicited adverse events (AEs) that occurred within 28 days post-vaccination were reported overall in 21.8% of 3,082 participants receiving IXCHIQ compared with 13.3% of 1,033 participants receiving placebo. Overall, most unsolicited AEs were graded as mild or moderate. Eighteen participants (0.6%) in the IXCHIQ arm and six (0.6%) in the placebo arm experienced at least one unsolicited AE that was graded severe. Unsolicited AEs were significantly more frequently considered related to the vaccination in the IXCHIQ arm (9.2% participants) than in the placebo arm (3.7% participants).

### Adolescents 12 to <18 years of age

In Study VLA1553-321, the proportion of participants who experienced unsolicited AEs within 28 days post-vaccination was similar in the IXCHIQ recipients regardless of serostatus.

### *Chikungunya virus baseline seronegative adolescents*

Unsolicited AEs that occurred within 28 days post-vaccination were reported in 39.5% of 408 baseline seronegative participants receiving IXCHIQ and 31.1% of 206 baseline seronegative participants receiving placebo. Overall, most unsolicited AEs were graded as mild or moderate. Five baseline seronegative participants (1.2%) in the IXCHIQ arm and none (0%) in the placebo arm experienced at least one unsolicited AE that was graded severe. Unsolicited AEs were significantly more frequently considered related to the vaccination in the IXCHIQ arm (9.6% of baseline seronegative participants) than in the placebo arm (0.5% of baseline seronegative participants).

- INDICATIONS
- CONTRAINDICATIONS
- SERIOUS WARNINGS AND PRECAUTIONS BOX
- DOSAGE AND ADMINISTRATION
- OVERDOSAGE
- DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING
- WARNINGS AND PRECAUTIONS
- ADVERSE REACTIONS 
- DRUG INTERACTIONS
- CLINICAL PHARMACOLOGY
- STORAGE, STABILITY AND DISPOSAL
- SPECIAL HANDLING INSTRUCTIONS
- PHARMACEUTICAL INFORMATION
- CLINICAL TRIALS
- MICROBIOLOGY
- NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY
- PATIENT MEDICATION INFORMATION

*Chikungunya virus baseline seropositive adolescents*

Unsolicted AEs that occurred within 28 days post-vaccination were reported in 38.3% of 94 baseline seropositive participants receiving IXCHIQ and 37.8% of 45 baseline seropositive participants receiving placebo. Overall, most unsolicted AEs were graded as mild or moderate. Five baseline seropositive participants (5.3%) in the IXCHIQ arm and three baseline seropositive participants (6.7%) in the placebo arm experienced at least one unsolicted AE that was graded severe. Unsolicted AEs considered related to vaccination occurred at similar rates in the IXCHIQ arm (1.1% of baseline seropositive participants) and the placebo arm (4.4% of baseline seropositive participants).

Specific categories of related unsolicted AEs of adults and adolescents are presented in Table 4 below.

**Table 4. Related Unsolicted Adverse Events Within 28 Days After a Single Vaccination With a Frequency ≥1% in at Least One Study Arm (Safety Population in Adults in the Study VLA1553-301 and in Baseline Seronegative Adolescents in Study VLA1553-321)**

Preferred Term (PT)	Study VLA1553-301		Study VLA1553-321	
	IXCHIQ (N=3,082) n (%)	Placebo (N=1,033) n (%)	IXCHIQ (N=408) n (%)	Placebo (N=206) n (%)
<b>Any Related Unsolicted Adverse Events</b>	<b>283 (9.2)</b>	<b>38 (3.7)</b>	<b>39 (9.6)</b>	<b>1 (0.5)</b>
Chills	51 (1.7)	2 (0.2)	3 (0.7)	Not reported
Neutropenia	31 (1.0)	1 (0.1)	4 (1.0)	Not reported
Fever	2 (0.1)	1 (0.1)	5 (1.2)	Not reported
Eye pain	5 (0.2)	Not reported	6 (1.5)	Not reported
Headache	7 (0.2)	5 (0.5)	4 (1.0)	Not reported

**Serious Adverse Events**

Adults ≥18 years of age

The proportions of participants who reported at least 1 serious adverse event within 6 months following administration was 1.5% (46/3,082) in the IXCHIQ group and 0.8% (8/1,033) in the placebo group. Overall, there were two serious adverse events (2/3,082 [0.1%]) requiring hospitalization that were considered to be related to IXCHIQ: 1 event of myalgia, and 1 event of hypovolemic hyponatremia and atrial fibrillation, both events showed full recovery.

A 58-year-old female with a history of fibromyalgia experienced severe myalgia, mild arthralgia, tachycardia and tachypnea, with onset 1 to 2 days after vaccination, was hospitalized 3 days after vaccination for 7 days, and fully recovered; myalgia resolved after 30 days.

A 66-year-old male experienced severe fever for 7 days, starting 4 days post-vaccination; he was hospitalized 9 days post-vaccination for 3 days and found to have atrial fibrillation, increased troponin, increased brain natriuretic peptide and hypovolemic hyponatremia, and fully recovered. This study participant was included in a subset of participants assessed for vaccine viremia 7 days after vaccination and was found to be viremic.

There were no related serious adverse events reported in the placebo group.

Adolescents 12 to <18 years of age

*Chikungunya virus baseline seronegative adolescents*

The proportions of baseline seronegative participants who reported at least one serious adverse event within 6 months following administration was 1.2% (5/408) in the IXCHIQ arm and 1.0% (2/206) in the placebo arm.

*Chikungunya virus baseline seropositive adolescents*

The proportions of baseline seropositive participants who reported at least one serious adverse event within 6 months following administration was 2.1% (2/94) in the IXCHIQ arm and 4.4% (2/45) in the placebo arm.

Overall, there was one serious adverse event (1/502 [0.2%]) requiring hospitalization that was considered to be related to IXCHIQ: 1 event of fever in a baseline seronegative participant who recovered fully.

A 13-year-old female who was baseline seronegative experienced fever of Grade 4 according to FDA grading scale (axillary body temperature: 40.2°C) starting two days after receiving IXCHIQ. The first normothermic temperature was reported four days after fever onset. As per protocol, any Grade 4 event required reporting as an SAE, no other seriousness criterion was met. This event was part of a chikungunya-like adverse reaction in combination with mild arthralgia in arms and hands, mild myalgia, and mild headache. The participant recovered without sequelae.

There were no related serious adverse events reported in the placebo group.

**Deaths and Adverse Events leading to Withdrawal from Study**

Three participants died during Study VLA1553-301 due to events independent of study procedures (coronary artery disease, COVID-19, and anoxic brain injury). None of the deaths was considered as related to IXCHIQ. Approximately 0.1% of participants who received IXCHIQ versus 0.2% in the placebo group discontinued their trial participation due to adverse events.

No participants died during the adolescent study VLA1553-321 up to 6 months post vaccination.

**8.2.1 Clinical Trial Adverse Reactions – Pediatrics**

Participants 11 years of age or younger were excluded from clinical trials with IXCHIQ.

**8.3 Less Common Clinical Trial Adverse Reactions**

Less common related, unsolicited adverse events, included:

Gastrointestinal: Diarrhoea.

General Disorders: Chills.

Haematologic Disorders: Neutropenia, leukopenia.

Immune system Disorders: Lymphadenopathy

Musculoskeletal and Connective Tissue Disorders: Back pain

Nervous System Disorders: Dizziness

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS



DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS



DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

## 8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

### Clinical Trial Findings

Laboratory data were analysed in the immunogenicity subset in Study VLA1553-301 in adults and Study VLA1553-321 in adolescents (see 14 CLINICAL TRIALS). Most hematology, chemistry and coagulation parameters were generally well balanced between the IXCHIQ and placebo arms in these studies. The exception were abnormal white cell counts, specifically leukocytes (all types of white blood cells), neutrophils and/or lymphocytes, which were more frequently observed in the IXCHIQ recipients compared with placebo recipients (Table 5 and Table 6). Most of these abnormal hematology parameters were of mild severity (grade 1) in both studies.

In Study VLA1553-301, of 186 participants with abnormal cell counts at the 7-day post-vaccination assessment, 92% (171/186) had available hematology results at the 28-day post-vaccination assessment, of which 88% (150 /171) were in the normal range. Three IXCHIQ recipients reported other significant non-serious severe adverse events: two events of neutropenia lasting for 13 or 20 days (both events were considered to be related to IXCHIQ) and one event of lymphopenia lasting for 22 days (the event was considered not related to IXCHIQ). All events resolved within 28-day post-vaccination.

Overall, changes in clinical laboratory test results were considered expected and consistent with a normal physiologic response to a live-attenuated viral vaccine.

**Table 5. Abnormal Hematology Results by Maximum Grade Post-vaccination in Adults (Immunogenicity Subset in Study VLA1553-301)**

Laboratory Parameter	IXCHIQ <sup>a</sup> (N=372) n (%)	Placebo <sup>a</sup> (N=125) n (%)
Leukocytes (decreased)	116 (32.0)	7 (5.8)
Neutrophils (decreased)	153 (42.3)	15 (12.4)
Lymphocytes (decreased)	85 (23.5)	9 (7.4)

<sup>a</sup> Percentages are based on the number of individuals with at least one postbaseline result.

**Table 6. Abnormal Hematology Results by Maximum Grade Post-vaccination in Baseline Seronegative Adolescents (Immunogenicity Subset in Study VLA1553-321)**

Laboratory Parameters	IXCHIQ <sup>a</sup> (N=268) n (%)	Placebo <sup>a</sup> (N=48) n (%)
Leukocytes (decreased)	46 (17.2)	3 (6.3)
Neutrophils (decreased)	109 (40.7)	14 (29.2)
Lymphocytes (decreased)	35 (13.1)	4 (8.3)

<sup>a</sup> Percentages are based on the number of individuals with at least one postbaseline result.

## 8.5 Post-Market Adverse Reactions

During post-marketing use, serious case reports were received from worldwide sources. Adverse events including those considered serious (medically important, leading to hospitalization or prolonging hospitalization) in individuals with onset within 30 days of receiving IXCHIQ are summarized in Table 7. Because post-marketing adverse events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate the frequency or establish a causal relationship to vaccine exposure.

**Table 7. Post-Market Adverse Reactions**

System/Organ Class	Adverse Event
Blood and lymphatic system disorder	Lymphadenopathy, thrombocytopenia (low platelets)
Cardiac disorders	Atrial flutter, heat palpitations, pericardial effusion, tachycardia, ventricular extrasystoles (extra beats)
Ear and labyrinth disorders	Tinnitus, vertigo
Eye disorders	Diplopia (double vision), photophobia (sensitivity to light)
Endocrine disorders	Exacerbation of secondary adrenal insufficiency
Gastrointestinal disorders	Anorexia, diarrhea
General disorders and administration site conditions	High fever, fatigue, sweats
Immune system disorders	Hemolytic uremic syndrome, pruritus (itching)
Injury, poisoning and procedural complications	Fall/injury
Investigations	Cerebral spinal fluid (CSF) positive by polymerase chain reaction (PCR) test for chikungunya virus in favour of vaccine strain, elevated C-reactive protein (CRP), elevated troponin
Metabolism and nutrition disorders	Dehydration, hyponatremia
Musculoskeletal and connective tissue disorders	Asthenia (physical weakness), arthritis (joint swelling), neck pain, neck stiffness, protracted joint pain, tendinitis
Nervous system disorders	Aseptic meningitis, Bell's palsy, encephalopathy, encephalitis, migraine, light-headedness, meningismus, pyramidal syndrome, syncope, trigeminal neuralgia
Psychiatric disorders	Behaviour disorder, hallucinations
Renal and urinary disorders	Acute kidney injury, nephrotic syndrome
Respiratory, thoracic and mediastinal disorders	Acute respiratory decompensation, dyspnea, fluid in lungs, pneumonitis
Skin and subcutaneous tissue disorders	Peri-orbital edema, skin eruption
Vascular disorders	Hypotension, phlebitis

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS



DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

During the vaccine campaign to address an outbreak in Réunion Island early in 2025, three deaths occurred within two weeks post-vaccination among frail elderly male individuals with multiple comorbidities (advanced neurological disorders and respiratory illness, pneumonia), due to medical decompensation (88 and 77 years of age) or confirmed encephalitis (84 years of age). One death was assessed as probably related to IXCHIQ vaccination by the local Health Authority. No deaths were reported in individuals receiving IXCHIQ for the purpose of international travel.

## TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS



DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

## 9 DRUG INTERACTIONS

### 9.2 Drug Interactions Overview

There are no data on the safety and immunogenicity following concomitant administration of IXCHIQ with other vaccines. During post-marketing use, some severe ICSR cases involved co-administration 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.

### 9.7 Drug Laboratory Test Interactions

Any laboratory testing within 2 weeks post-vaccination with IXCHIQ may result in transient abnormalities in results, especially among hematology parameters.

## TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS



CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

**10 CLINICAL PHARMACOLOGY**

**10.1 Mechanism of Action**

The exact mechanism of protection has not been determined. IXCHIQ elicits CHIKV-specific immune responses against all globally circulating chikungunya virus (CHIKV) genotypes.

**10.2 Pharmacodynamics**

Clinical studies with IXCHIQ included immunogenicity assessments to characterize the immune response to IXCHIQ. Immunogenicity endpoints were used as surrogate endpoints supporting the evaluation of clinical efficacy (see 13 CLINICAL TRIALS).

**10.3 Pharmacokinetics**

**Viremia:** The phase I study (Study VLA1553-101) assessed the kinetics of vaccine viremia on Day 3, Day 7 and Day 14 following single vaccination with IXCHIQ at three intramuscular dose levels ( $3.2 \times 10^3$  TCID<sub>50</sub>,  $3.2 \times 10^4$  TCID<sub>50</sub>, and  $3.2 \times 10^5$  TCID<sub>50</sub>) in healthy adults (see 14 CLINICAL TRIALS). The middle dose ( $3.2 \times 10^4$  TCID<sub>50</sub> or  $4.5 \log_{10}$  TCID<sub>50</sub>) is within the approved dose range ( $3.6 - 4.6 \log_{10}$  TCID<sub>50</sub>) of IXCHIQ. The viral titer in all study groups was the highest on Day 3, sharply dropped by about 85% on Day 7 and became undetectable on Day 14. The plasma viral titer was vaccine dose-dependent with mean viral RNA titer at 73,601.2 GCE/mL, 89,353.7 GCE/mL and 229,224.1 GCE/mL on Day 3 following vaccination at the three ascending dose level, respectively. Note: the administered viral doses are too low to be detectable in plasma if the virus does not replicate in the body.

One participant shed virus in urine in the low dose group on Day 7.

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION


OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY 

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

## 11 STORAGE, STABILITY AND DISPOSAL

Store vial with lyophilized powder and diluent in a refrigerator at 2°C to 8°C. DO NOT FREEZE. Do not use the vaccine after the expiration date shown on the vial label. Store in the original package.

After reconstitution, administer IXCHIQ immediately. If not used immediately, store the reconstituted vaccine at room temperature and administer within 30 minutes. DO NOT FREEZE RECONSTITUTED VACCINE.

Discard reconstituted vaccine, if not used within 30 minutes.

### TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION



## 12 SPECIAL HANDLING INSTRUCTIONS

Not applicable.

### TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS



PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

## PART II: SCIENTIFIC INFORMATION

### 13 PHARMACEUTICAL INFORMATION

#### Drug Substance

Proper name: Live Attenuated chikungunya La Reunion strain (LR-CHIKV clone LR2006 OPY1)

#### Product Characteristics:

IXCHIQ, chikungunya vaccine, live-attenuated, is a lyophilized powder reconstituted with sterile water to form a sterile solution for intramuscular injection. Each 0.5 mL dose of the vaccine contains not less than  $3.0 \log_{10}$  TCID<sub>50</sub> of live attenuated chikungunya virus.

The vaccine is produced in Vero cells. Viral harvests are pooled, clarified, concentrated and purified. The purified virus solution is further sterile filtered, aliquoted and stored at deep frozen conditions until formulation. The Vero cells, Viral Harvests, Drug Substance and Excipients used in manufacturing are all tested to provide assurance that the final product is free of potential adventitious agents.

## TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

## 14 CLINICAL TRIALS

### 14.1 Trial Design and Study Demographics

**Table 7: Summary of patient demographics for pivotal clinical trials for IXCHIQ**

<b>Study #</b>	<b>VLA1553-301</b>
<b>Study design</b>	Double-blind, randomized placebo-controlled
<b>Dosage, route of administration and duration</b>	IXCHIQ 1×10 <sup>4</sup> TCID <sub>50</sub> per 0.5 mL, or placebo (phosphate buffered saline, PBS) Intramuscular injection Single dose, 6 month follow up
<b>Study subjects (n)</b>	IXCHIQ: 3,093 (3,045 planned) Immunogenicity subset: 375 Placebo (phosphate buffered saline): 1,035 (1,015 planned) Immunogenicity subset: 126
<b>Mean age (Range)</b>	45.0 years (18.0-94.0)
<b>Sex (%)</b>	1,864 M (45.3%) 2,251 F (54.7%)
<b>Study #</b>	<b>VLA1553-321</b>
<b>Study design</b>	Double-blind, randomized placebo-controlled
<b>Dosage, route of administration and duration</b>	IXCHIQ 1×10 <sup>4</sup> TCID <sub>50</sub> per 0.5 mL, or placebo (phosphate buffered saline, PBS) Intramuscular injection Single dose, 12 month follow up
<b>Study subjects (n)</b>	IXCHIQ baseline seronegative: 408 (400 planned) IXCHIQ baseline seropositive: 94 (100 planned) IXCHIQ baseline seronegative Immunogenicity subset: 268 IXCHIQ baseline seropositive Immunogenicity subset: 60 Placebo baseline seronegative: 206 (200 planned) Placebo baseline seropositive: 45 (50 planned) Placebo baseline seronegative Immunogenicity subset: 48 Placebo baseline seropositive Immunogenicity subset: 8
<b>Mean age (Range)</b>	14.5 years (12.0-17.0)
<b>Sex (%)</b>	348 M (46.2%) 406 F (53.8%)

Study VLA1553-301, conducted in United States, was a multicenter, prospective, randomized, double-blinded, placebo-controlled pivotal clinical study assessing the immunogenicity and safety in generally healthy individuals 18 years and above after vaccination with a single dose of IXCHIQ. Almost all participants were negative for CHIKV-specific neutralizing antibodies at baseline (99.9% in the VLA1553 group

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY


PATIENT MEDICATION INFORMATION

and 99.7% in the placebo group). 4,128 participants were randomized, allocated in approximately 3:1 ratio to VLA1553 arm (n=3,093) or placebo arm (n=1,035) and stratified by age, i.e. 18 to 64 years (n=3,652) and 65 years of age or above (n=463). The first 501 randomized participants were included in the immunogenicity subset (IXCHIQ: n=375 and placebo: n=126).

Study VLA1553-321, conducted in Brazil, was a multicenter, prospective, randomized, double-blinded, placebo-controlled pivotal clinical trial, to evaluate immunogenicity and safety in healthy adolescents (12 to 17 years old) after vaccination with a single dose of IXCHIQ. According to 50% plaque reduction in a micro plaque reduction neutralization ( $\mu$ PRNT<sub>50</sub>) assay, 81.4% and 18.4% of the participants were seronegative and seropositive, respectively, for CHIKV-specific neutralizing antibodies at baseline. 754 participants were randomized in approximately 2:1 ratio to IXCHIQ (n=502) or placebo (n=252) and stratified according to baseline serostatus for CHIKV-specific neutralizing antibodies. The first 384 of the randomized participants were included in the immunogenicity subset (IXCHIQ-seronegative: n=268; placebo-seronegative: n=48; IXCHIQ-seropositive: n=60; placebo-seropositive: n=8). 78 participants in the immunogenicity subset constituted the viremia subset (IXCHIQ-seronegative: n=43; placebo-seronegative: n=20; IXCHIQ-seropositive: n=9; placebo-seropositive: n=9). Treatment randomization was not stratified by immunogenicity and viremia subsets, rather, the subset inclusion was stratified based on treatment allocation.

**Study VLA1553-301 in adults and Study VLA1553-321 in adolescents share the following study design features.**

Vaccination was performed with a single intramuscular dose of IXCHIQ (1×10<sup>4</sup> 50% tissue culture infectious dose [TCID<sub>50</sub>]) or placebo (phosphate buffered saline, PBS) on Day 1. In both studies, immunogenicity samples were collected from all participants at baseline and on Days 8, 29, 85, and 180 (samples were only analyzed for participants in the immunogenicity subset) and also on Day 365 in Study VLA1553-321 (only collected and analyzed in the immunogenicity subset). In both studies, clinical laboratory samples (clinical chemistry, hematology, urinalysis, coagulation) were collected only from participants in the immunogenicity subset at baseline (Day 1) and on Days 8, 29, 85, and 180. Viremia plasma samples were obtained from all participants on Days 1, 8, and 29 in both studies and also on Days 85, 180 and 365 (only in the immunogenicity subset) in Study VLA1553-321. The primary endpoint was seroresponse rate (SRR), i.e. proportion of participants with a serum CHIKV-specific neutralizing antibody level defined as  $\mu$ PRNT<sub>50</sub>≥150 at 28 days post-vaccination. Based on the results of a study of passive transfer of human anti-IXCHIQ sera in non-human primates (see 16. NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY), a CHIKV-specific neutralizing antibody level that is 150  $\mu$ PRNT<sub>50</sub> or higher is considered seroprotective. The primary immunogenicity analysis compared the SRR against a non-acceptance threshold of 70%. Safety data collection captured solicited AEs until Day 11 and unsolicited AEs up to Day 180 and Month 12 (after Day 180, only adverse events of special interest and serious adverse events were collected, and this was done in the immunogenicity subset) in Study VLA1553-301 and Study VLA1553-321, respectively.

- INDICATIONS
- CONTRAINDICATIONS
- SERIOUS WARNINGS AND PRECAUTIONS BOX
- DOSAGE AND ADMINISTRATION
- OVERDOSAGE
- DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING
- WARNINGS AND PRECAUTIONS
- ADVERSE REACTIONS
- DRUG INTERACTIONS
- CLINICAL PHARMACOLOGY
- STORAGE, STABILITY AND DISPOSAL
- SPECIAL HANDLING INSTRUCTIONS
- PHARMACEUTICAL INFORMATION
- CLINICAL TRIALS 
- MICROBIOLOGY
- NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY
- PATIENT MEDICATION INFORMATION

Study VLA1553-303 is a prospective, multicenter, open-label Phase 3b, single arm clinical trial evaluating antibody persistence and long-term safety (SAEs only) in 363 adult participants who had participated in Study VLA1553-301 and voluntarily agreed to be recruited into Study VLA1553-303. All participants were asked to visit the trial site on Day 180 of VLA1553-301 and then have annual follow-up visits for 10 years for immunogenicity sampling. SAEs were also assessed until Year 2 in all participants. Data are available up to Year 2.

## 14.2 Study Results

### Adults ≥18 years of age

Seroresponse was selected as a surrogate immunogenicity endpoint of efficacy. It is defined as achieving a virus neutralizing antibody  $\mu$ PRNT<sub>50</sub> titer ≥150, which was considered to predict a clinical benefit. This is based on nonclinical data from a non-human primate pharmacology study showing that animals treated with immune sera from clinical samples collected in Study VLA1553-101 were protected against mild CHIKV disease induced by challenge with a WT CHIKV strain (See Study VAC1816 02 in 16. NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY). Pre challenge neutralizing antibody titer level about 150 resulted in undetectable virus during 14 days after the challenge.

In Study VLA1553-301, the primary immunogenicity endpoint was the seroresponse rate (proportion of participants who had seroresponse in a study group) at 28 days post-vaccination. Key secondary immunogenicity endpoint was immune response as measured by CHIKV-specific neutralizing antibody titers on Day 8, Day 29, Day 85, and at Month 6 post-vaccination as determined by  $\mu$ PRNT<sub>50</sub> in  $\mu$ PRNT assay.

#### Seroresponse Rate

The seroresponse rate 28 days post-vaccination after a single dose of IXCHIQ in adults is presented in Table 8. The seroresponse rate 180 days after a single dose of IXCHIQ was 96.3% (95% CI: 93.1, 98.3).

**Table 8: Seroresponse Rates 28 days post-vaccination, as Determined by  $\mu$ PRNT Assay, in Adults in Study VLA1553-301 (PP Population)**

Study	Study VLA1553-301	
	Placebo	IXCHIQ
	N=96	N=266
	(n (%) [95% CI])	(n (%) [95% CI])
<b>Day 29 (28 days post-vaccination)</b>	0 (0) [0.0, 3.8]	263 (98.9) [96.7, 99.8]*

Abbreviations: CI=confidence interval;  $\mu$ PRNT=micro plaque reduction neutralization test; PP=per-protocol (population).

\* Success criterion: lower bound of the 95% confidence interval for seroresponse rate >70%

#### Geometric Mean Titer (GMT)

The geometric mean titer 28 days and 6 months post-vaccination after a single dose of IXCHIQ in adults is presented in Table 9. GMT was 3361.6 on Day 29 (28 days post-vaccination) and dropped by about 78% to 752.1 at 6 months post-vaccination, remaining above the seroresponse threshold of ≥150  $\mu$ PRNT<sub>50</sub>.

**Table 9: GMT of Serum CHIKV-specific Neutralizing Antibodies up to 6 Months Post-vaccination, as Determined by  $\mu$ PRNT Assay, in Adults in Study VLA1553-301 (PP Population)**

Study	Study VLA1553-301	
	Placebo	IXCHIQ
Treatment	<b>N=96</b>	<b>N=266</b>
	GMT	GMT [95% CI]
<b>Day 1 (baseline, pre-vaccination)</b>	10.0	10.0 [10.00, 10.00]
<b>Day 29 (28 days post-vaccination)</b>	10.1	3,361.6 [2,993.83, 3,774.45]
<b>Day 180 (6 months post-vaccination)</b>	10.0	752.1 [665.91, 849.52]

Abbreviations: CHIKV=chikungunya virus; GMT=Geometric Mean Titer as measured in  $\mu$ PRNT<sub>50</sub>;  $\mu$ PRNT=micro plaque reduction neutralization test; PP=per-protocol (population).

Antibody persistence in adults

Persistence of the immune response was evaluated 12 and 24 months post-vaccination in VLA1553-303. GMTs and seroresponse rates at 12 and 24 months in adults are included in Table 10.

The proportion of participants with a CHIKV-specific neutralizing antibody level  $\geq 150$   $\mu$ PRNT<sub>50</sub> was 99.5% (183/184) and 97.1% (268/276), respectively at 12 and 24 months post-vaccination. GMT decreased from 3,361.6 at 28 days post-vaccination from study VLA1553-301 (Table 9) to 1,070.3 at 12 months and 819.5 at 24 months, with GMTs remaining above the seroresponse threshold of  $\geq 150$   $\mu$ PRNT<sub>50</sub> (Table 10). In contrast, CHIKV-specific antibodies elicited by wide-type CHIKV remained a high pre-vaccination level for a prolonged period in baseline seropositive adolescents after vaccination with placebo in Study VLA1553-321 (Table 13).

Note: Study VLA1553-301 was the parent study, from where all participants in Study VLA1553-303 were recruited to continue annual follow-up for ten years after vaccination in Study VLA1553-301 (see 14.1 Trial Design and Study Demographics).

**Table 10: GMT of Serum CHIKV-specific Neutralizing Antibodies and Seroresponse Rate up to 24 Months Post-vaccination, as Determined by  $\mu$ PRNT Assay, in Adults in Study VLA1553-303 (PP Population)**

Study	Study VLA1553-303	
	IXCHIQ	
Treatment	<b>N=339</b>	
	GMT (n [95%CI])	Seroresponse (n (%) [95%CI])
<b>Year 1 (12 months post-vaccination)</b>	1,070.3 [935.35, 1224.64]	183 (99.5) [97.0, 100.0]
<b>Year 2 (24 months post-vaccination)</b>	819.5 [731.74, 917.81]	268 (97.1) [94.4, 98.7]

Abbreviations: CHIKV=chikungunya virus; GMT=Geometric Mean Titer as measured in  $\mu$ PRNT<sub>50</sub>;  $\mu$ PRNT= micro plaque reduction neutralization test; PP=per-protocol (population).

- INDICATIONS
- CONTRAINDICATIONS
- SERIOUS WARNINGS AND PRECAUTIONS BOX
- DOSAGE AND ADMINISTRATION
- OVERDOSAGE
- DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING
- WARNINGS AND PRECAUTIONS
- ADVERSE REACTIONS
- DRUG INTERACTIONS
- CLINICAL PHARMACOLOGY
- STORAGE, STABILITY AND DISPOSAL
- SPECIAL HANDLING INSTRUCTIONS
- PHARMACEUTICAL INFORMATION
- CLINICAL TRIALS
- MICROBIOLOGY
- NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY
- PATIENT MEDICATION INFORMATION

There was no meaningful difference in the seroresponse rate or GMTs in adults aged 18 to 64 years and those aged ≥65 years up to 24 months post-vaccination.

**Adolescents 12 to <18 years of age**

**Seroresponse Rate in Baseline Seronegative Adolescents**

The seroresponse rate 28 days post-vaccination after a single dose of IXCHIQ or placebo in baseline seronegative adolescents is presented in Table 11.

**Table 11: Seroresponse Rates 28 days and 6 Months Post-vaccination, as Determined by μPRNT Assay, in Baseline Seronegative Adolescents in Study VLA1553-321 (PP Population)**

Study	Study VLA1553-321	
	Placebo	IXCHIQ
	<b>N=42</b>	<b>N=251</b>
	<b>(n (%) [95%CI])</b>	
<b>Day 29 (28 days post-vaccination)</b>	1 (2.4) [0.1, 12.6]	248 (98.8) [96.5, 99.8]*
<b>Day 180 (6 months post-vaccination)</b>	0 (0) [0.0, 9.0]	232 (99.1) [96.9, 99.9]

Abbreviations: CI=confidence interval; μPRNT=micro plaque reduction neutralization test; PP=per-protocol (population).

\* Success criterion: lower bound of the 95% confidence interval for seroresponse rate >70%.

The seroresponse rate 180 days after a single dose of IXCHIQ in baseline seronegative adolescents was 99.1% (95% CI: 96.9, 99.9).

**Geometric Mean Titer (GMT) in Baseline Seronegative Adolescents**

The geometric mean titers 28 days and 6 months post-vaccination after a single dose of IXCHIQ or placebo in baseline seronegative adolescents are presented in Table 12.

**Table 12: GMT of Serum CHIKV-specific Neutralizing Antibodies up to 6 Months Post-vaccination, as Determined by μPRNT Assay, in Baseline Seronegative Adolescents in Study VLA1553-321 (PP Population)**

Study	Study VLA1553-321	
	Placebo	IXCHIQ
	<b>N=42</b>	<b>N=251</b>
	GMT (95% CI)	GMT (95% CI)
<b>Day 1 (baseline, pre-vaccination)</b>	11.7 (10.46, 13.17)	10.6 (10.31, 10.89)
<b>Day 29 (28 days post-vaccination)</b>	12.3 (9.63, 15.79)	3,855.9 (3432.05, 4331.98)
<b>Day 180 (6 months post-vaccination)</b>	10.0 (10.00, 10.00)	1,399.0 (1257.01, 1556.98)

Abbreviations: CHIKV=chikungunya virus; GMT=Geometric Mean Titer as measured in μPRNT<sub>50</sub>; μPRNT=micro plaque reduction neutralization test; PP=per-protocol (population).

- INDICATIONS
- CONTRAINDICATIONS
- SERIOUS WARNINGS AND PRECAUTIONS BOX
- DOSAGE AND ADMINISTRATION
- OVERDOSAGE
- DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING
- WARNINGS AND PRECAUTIONS
- ADVERSE REACTIONS
- DRUG INTERACTIONS
- CLINICAL PHARMACOLOGY
- STORAGE, STABILITY AND DISPOSAL
- SPECIAL HANDLING INSTRUCTIONS
- PHARMACEUTICAL INFORMATION
- CLINICAL TRIALS
- MICROBIOLOGY
- NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY
- PATIENT MEDICATION INFORMATION

The GMT on Day 29 after a single dose of IXCHIQ (28 days post-vaccination) in baseline seronegative adolescents was 3855.9, which is at a similar level as the baseline GMT (3097.1) in the baseline seropositive adolescents (see Table 13). However, the GMT at 6 months post-vaccination in the baseline seronegative adolescents reduced to 1399.0, a 64% drop from the GMT value on 28 days post-vaccination.

**Geometric Mean Titer (GMT) in Baseline Seropositive Adolescents**

The geometric mean titer 28 days and 6 months post-vaccination after a single dose of IXCHIQ or placebo in baseline seropositive adolescents is presented in Table 13.


**Table 13: GMT of Serum CHIKV-specific Neutralizing Antibodies up to 6 Months Post-vaccination, as Determined by  $\mu$ PRNT Assay, in Baseline Seropositive Adolescents in Study VLA1553-321 (PP Population)**

Study	Study VLA1553-321	
	Placebo	IXCHIQ
	<b>N=6</b>	<b>N=52</b>
	<b>GMT (95%CI)</b>	<b>(GMT 95%CI)</b>
<b>Day 1 (baseline, pre-vaccination)</b>	3,409.0 (2244.36, 5178.13)	3,097.1 (2324.90, 4125.89)
<b>Day 29 (28 days post-vaccination)</b>	3,339.2 (2394.37, 4656.76)	3,886.5 (3063.40, 4930.87)
<b>Day 180 (6 months post-vaccination)</b>	4,745.8 (2837.32, 7938.13)	3,504.7 (2623.29, 4682.28)

Abbreviations: CHIKV=chikungunya virus; GMT=Geometric Mean Titer as measured in  $\mu$ PRNT<sub>50</sub>;  $\mu$ PRNT=micro plaque reduction neutralization test; PP=per-protocol (population).

GMT in the placebo group of baseline seropositive adolescents did not significantly change from the high baseline level (3,409) during the 6-month study period, suggesting there is a sustained high level of CHIKV-specific neutralizing antibodies against wide-type CHIKV after prior exposure to CHIKV.

The baseline GMT in the IXCHIQ group of baseline seropositive adolescents was 3,097.1. The GMTs on 28 days and 6 months post-vaccination in these adolescents were at a level similar to that at baseline, showing that there appears no boosting effect to elicit CHIKV-specific antibody response by vaccination with IXCHIQ in baseline seropositive adolescents.

- INDICATIONS
- CONTRAINDICATIONS
- SERIOUS WARNINGS AND PRECAUTIONS BOX
- DOSAGE AND ADMINISTRATION
- OVERDOSAGE
- DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING
- WARNINGS AND PRECAUTIONS
- ADVERSE REACTIONS
- DRUG INTERACTIONS
- CLINICAL PHARMACOLOGY
- STORAGE, STABILITY AND DISPOSAL
- SPECIAL HANDLING INSTRUCTIONS
- PHARMACEUTICAL INFORMATION
- CLINICAL TRIALS 
- MICROBIOLOGY
- NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY
- PATIENT MEDICATION INFORMATION

## 15 MICROBIOLOGY

No microbiological information is required for this drug product.

### TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY



NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

## 16 NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

### **Animal Toxicology Studies**

One repeat dose toxicity study in rabbits and one pre- and post-natal developmental study in female Sprague-Dawley rats (see below) were conducted in animal toxicology studies to investigate the safety of IXCHIQ vaccine. There were no significant safety issues identified in these studies. However, unlike humans, rats and rabbits have strong natural resistance against CHIKV infection.

**General Toxicology:** In a repeat dose toxicity study, the intramuscular injection of  $3.8 \times 10^5$  TCID<sub>50</sub>/dose of IXCHIQ to rabbits on 2 occasions at a 2-week interval was well-tolerated both systemically and locally. IXCHIQ was associated with an inflammatory response and reactions at the administration sites. The findings resolved after a 30-day recovery.

**Carcinogenicity:** IXCHIQ has not been evaluated for carcinogenic potential.

**Genotoxicity:** IXCHIQ has not been evaluated for mutagenic potential.

### **Reproductive and Developmental Toxicology**

The effect of IXCHIQ vaccine on female fertility, reproductive performance, and pre-/post-natal development was evaluated in one pre- and post-natal developmental toxicity study using pregnant rats. The animals were intramuscularly administered with IXCHIQ ( $1.9 \times 10^4$  TCID<sub>50</sub>/rat or 4.3 log<sub>10</sub> TCID<sub>50</sub>/rat) or placebo once 15 days prior to gestation and once on gestation Day 6. No significant adverse effects on mating, fertility, pregnancy, parturition, lactation, embryo-fetal or pre-weaning development were observed except that the rate of post-implantation loss in IXCHIQ-treated animals in the littering phase was statistically higher than that in placebo control animals but within the history range of the parameter obtained in the testing facility.

### **Pharmacology Studies in Non-human Primates (NHPs)**

A study in non-human primates, *Macaca fascicularis*, (Study PHY1802-02) compared viral replication, viral shedding, presence of viral RNA in relevant tissues, inflammatory responses, and clinical impacts between IXCHIQ and its wild-type (WT) CHIKV parent strain, LR2006-OPY1, following the same intramuscular dose of  $3.2 \times 10^6$  TCID<sub>50</sub>. This dose is vastly higher than the estimated maximum amount of CHIKV that one CHIKV-vector mosquito may deliver to human. The kinetic profiles of plasma viremia were similar for WT CHIKV and IXCHIQ with viral titers peaking on day 2 and dropping by >99.9% (about 4.2 logs) until day 6 after virus injection. However, the geometric mean peak titer for IXCHIQ was reduced by about 99.8% (2.8 logs) compared to that for WT CHIKV, indicating that replication of IXCHIQ in the NHPs was attenuated by about 99.8% compared to that of its parent WT CHIKV strain. The WT CHIKV-treated animals experienced fever and lymphopenia, the hallmarks of CHIKV illness, but only in mild to moderate severity and a short duration. Despite being heavily attenuated in replication in the animals compared to WT CHIKV, IXCHIQ induced fever and lymphopenia in a similar or slightly lesser extent in severity and/or duration, if any, compared to those seen in the WT CHIKV-treated animals.

## TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY



PATIENT MEDICATION INFORMATION

A non-human primate pharmacology study (Study VAC1816 02) investigated protective effects of pooled human sera from IXCHIQ -vaccinated subjects in the Phase I clinical study (VLA1553-101) against CHIKV infection induced by challenge with WT CHIKV strain LR2006-OPY1. Challenge with a subcutaneous dose ( $1.5 \times 10^4$  TCID<sub>50</sub>) of WT CHIKV in the animals resulted in a significant level of plasma viremia with a geometric mean peak titer of  $1.3 \times 10^9$  GCE/ml but only induced mild clinical signs of chikungunya disease, i.e. mild fever and lymphopenia with short duration (less than 2 days for lymphopenia). Intravenous transfer of pooled sera of IXCHIQ -vaccinated subjects in the Phase I clinical study (VLA1553-101) in the animals provided protection against CHIKV infection induced by subsequent challenge of WT CHIKV. In the animals who had plasma human CHIKV-specific neutralizing antibody titer around 150  $\mu$ PRNT<sub>50</sub>, there was no detectable plasma CHIKV RNA, no clinical signs of chikungunya disease including fever or modification of blood parameters. and no inflammatory cytokine responses after the WT CHIKV challenge, indicating that human CHIKV-specific neutralizing antibody titer around 150  $\mu$ PRNT<sub>50</sub> in plasma of NHPs provided full protection against mild chikungunya disease induced by WT CHIKV in the animals.

## TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY



PATIENT MEDICATION INFORMATION

# PATIENT MEDICATION INFORMATION

## READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

### IXCHIQ

#### Chikungunya Vaccine, Live attenuated, Powder for Solution for Intramuscular Injection

Read this carefully before you receive **IXCHIQ**. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **IXCHIQ**.

#### What is **IXCHIQ** used for?

- **IXCHIQ** is a vaccine for intramuscular injection for use in individuals 12 years of age and older to help protect against chikungunya virus (CHIKV).

#### How does **IXCHIQ** work?

**IXCHIQ** stimulates your immune system to make substances known as antibodies which fight the chikungunya virus. If a vaccinated person comes into contact with chikungunya virus their body can fight off the virus. Following a single intramuscular dose of **IXCHIQ**, it usually takes two to four weeks to be protected against chikungunya virus. As with all vaccines, 100% protection is not guaranteed.

#### What are the ingredients in **IXCHIQ**?

Medicinal ingredients: Purified live-attenuated chikungunya virus (CHIKV)

Non-medicinal ingredients: D-Sorbitol, L-Methionine, Magnesium Chloride, Potassium phosphate, Recombinant Human Albumin (rHA), Sucrose, Trisodium citrate di-hydrate.

#### **IXCHIQ** comes in the following dosage forms:

**IXCHIQ**, chikungunya vaccine, live, attenuated, is a lyophilized powder reconstituted with sterile water to form a sterile solution for intramuscular injection. Each 0.5 mL dose of the vaccine contains not less than  $3.0 \log_{10}$  TCID<sub>50</sub> of live attenuated chikungunya virus.

#### Do not use **IXCHIQ** if:

- you have or if it is suspected that you have an immunodeficiency or immunosuppression (e.g., from malignancies such as cancers arising from abnormal blood or bone marrow cells and solid tumors, recent chemotherapy, immunodeficiency from birth, long-term immunosuppressive therapy) for chronic conditions such as autoimmune disorders or organ transplants, or HIV infection with immunocompromised state);
- you are allergic to any of the ingredients in the vaccine (see What are the ingredients in **IXCHIQ**?)
- you are pregnant. Women of child-bearing potential should be advised to avoid pregnancy for one month following vaccination.

## TABLE OF CONTENTS

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

**To help avoid side effects and ensure proper use, talk to your healthcare professional before you take IXCHIQ. Talk about any health conditions or problems you may have, including if you:**

- have any conditions impacting your overall fitness, and the stability of these conditions.
- have a weakened immune system, for example, due to a genetic defect, HIV infection, or certain medications such as cancer treatment.
- have a bleeding disorder or a reduction in blood platelets, which increases risk of bleeding or bruising (thrombocytopenia) and cannot receive injections in the arm.
- currently have any illness with a fever of more than 38.0 °C.
- have had an allergic reaction to a component of IXCHIQ.
- take any medicines, even those you can buy over the counter.

**Serious warnings and Precautions:**

- Available post-marketing data suggest that individuals 65 years of age and older who are medically frail with multiple chronic medical conditions may have an increased risk for serious adverse reactions following recent vaccination with IXCHIQ.
- Severe reactogenicity or chikungunya-like adverse reactions may lead to a worsening of the general condition including a general feeling of discomfort and decreased appetite, worsening of preexisting diseases, confusional state, encephalopathy (disturbance of brain function), or encephalitis (inflammation of the brain), leading to falls, hospitalisation and death. Vaccinees should promptly seek medical attention if they experience, after vaccination, symptoms suggestive of severe reactogenicity or severe chikungunya-like adverse reactions.
- For cases received post-marketing indicative of Chikungunya-like adverse reactions, the most frequent symptoms reported in combination with fever were headache (51% of reports), arthralgia (41%), fatigue (38%) and myalgia (35%), pain (19%) and chills (19%). This mostly aligns with findings from clinical trials, with no notable differences observed.
- As with all injectable vaccines, appropriate medical treatment and supervision should always be available to treat possible anaphylactic reactions following the administration of the vaccine.
- IXCHIQ must never be injected into a vein or any blood vessel.
- As with any other vaccine, vaccination with IXCHIQ may not result in protection in all people.
- Like other intramuscular injections, this vaccine should not be administered to persons with thrombocytopenia, hemophilia or other bleeding disorders.
- People with a medically-confirmed weak immune system (immunodeficiency) or taking medicines that can undermine the immune system (e.g., high-dose corticosteroids, drugs for rheumatoid arthritis or cancer drugs), IXCHIQ should not be given as it is a live vaccine.

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION

**Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.**

**The following may interact with IXCHIQ:**

- 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.

**How to take IXCHIQ:**

- IXCHIQ is given by a healthcare professional in a healthcare setting. It is given as an injection in the upper arm muscle in individuals 12 years of age and older.
- You should consult your health care provider on the duration of protection of IXCHIQ prior to potential re-exposure to CHIKV.
- You should still protect yourself from mosquito bites even if you have received the IXCHIQ vaccine.
- IXCHIQ does not protect against other diseases transmitted by mosquitoes.

**Usual dose:**

IXCHIQ is given as a single injection in the upper arm muscle.

**Overdose:**

There are no reported cases of overdose with IXCHIQ.

If you think you, or a person you are caring for, have taken too much IXCHIQ, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

**What are possible side effects from using IXCHIQ?**

The most common side effects of IXCHIQ are headache, fatigue, muscle pain, joint pain, fever and nausea, which are also common symptoms of chikungunya disease. They are usually mild to moderate and go away on their own after a short time. In some individuals, these side effects can interfere with daily activities, may persist for several weeks, might require medical intervention and, in rare cases, could lead to hospitalization.

The most common injection site reactions are tenderness and pain. Redness, hardening, and swelling may also occur. In addition, rare serious side effects shown in the following table may occur.

- INDICATIONS
- CONTRAINDICATIONS
- SERIOUS WARNINGS AND PRECAUTIONS BOX
- DOSAGE AND ADMINISTRATION
- OVERDOSAGE
- DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING
- WARNINGS AND PRECAUTIONS
- ADVERSE REACTIONS
- DRUG INTERACTIONS
- CLINICAL PHARMACOLOGY
- STORAGE, STABILITY AND DISPOSAL
- SPECIAL HANDLING INSTRUCTIONS
- PHARMACEUTICAL INFORMATION
- CLINICAL TRIALS
- MICROBIOLOGY
- NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

**Serious side effects and what to do about them**

Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
<b>RARE</b>			
<ul style="list-style-type: none"> <li>• Difficulty breathing</li> <li>• Hoarseness or wheezing</li> <li>• Hives</li> <li>• Dizziness, weakness or fast heartbeat</li> </ul>		<u>X</u>	<u>X</u>

Some people who have received IXCHIQ have experienced rare serious side effects similar to complications that can occur with chikungunya virus (similar to section 8.2). Serious side effects that have been reported include:

- Atrial Flutter (abnormal heart rate)
- Rapid heart rate
- Aseptic meningitis (inflammation of the membranes covering the brain and spinal cord that is not due to a bacterial infection)
- Encephalopathy (brain dysfunction with symptoms such as confusion and impaired memory)
- Encephalitis (inflammation of brain tissue) that resulted in death

People 65 years of age and older who are medically frail with multiple chronic (long-term) unstable medical conditions might have an increased risk for these types of serious side effects after receiving IXCHIQ.

These are not all the possible side effects you may have when taking IXCHIQ. If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

- INDICATIONS
- CONTRAINDICATIONS
- SERIOUS WARNINGS AND PRECAUTIONS BOX
- DOSAGE AND ADMINISTRATION
- OVERDOSAGE
- DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING
- WARNINGS AND PRECAUTIONS
- ADVERSE REACTIONS
- DRUG INTERACTIONS
- CLINICAL PHARMACOLOGY
- STORAGE, STABILITY AND DISPOSAL
- SPECIAL HANDLING INSTRUCTIONS
- PHARMACEUTICAL INFORMATION
- CLINICAL TRIALS
- MICROBIOLOGY
- NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

**Reporting Suspected Side Effects for Vaccines**

**For the general public:** Should you experience a side effect following immunization, please report it to your healthcare professional.

Should you require information related to the management of the side effect, please contact your healthcare professional. The Public Health Agency of Canada, Health Canada and Valneva cannot provide medical advice.

**For healthcare professionals:** If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (<http://www.phac-aspc.gc.ca/im/ae-fi-essi-form-eng.php>) and send it to your local Health Unit.

**Storage:**

Store in a refrigerator at 2°C to 8°C. DO NOT FREEZE. Do not use the vaccine after the expiration date shown on the vial label. Store in the original package.

After reconstitution, administer IXCHIQ immediately. If not used immediately, store the reconstituted vaccine at room temperature and administer within 30 minutes. DO NOT FREEZE RECONSTITUTED VACCINE.

Discard reconstituted vaccine, if not used within 30 minutes.

Keep out of reach and sight of children.

**If you want more information about IXCHIQ:**

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website [www.valneva.ca](http://www.valneva.ca), or by calling Medical Information at Valneva Canada Inc. at 1-855-356-0831. Business hours: 9:00 a.m. to 5:00 p.m. Eastern Time, Monday to Friday.
- This leaflet was prepared by Valneva Austria GmbH.

Last Revised January, 2026

INDICATIONS

CONTRAINDICATIONS

SERIOUS WARNINGS AND PRECAUTIONS BOX

DOSAGE AND ADMINISTRATION

OVERDOSAGE

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

WARNINGS AND PRECAUTIONS

ADVERSE REACTIONS

DRUG INTERACTIONS

CLINICAL PHARMACOLOGY

STORAGE, STABILITY AND DISPOSAL

SPECIAL HANDLING INSTRUCTIONS

PHARMACEUTICAL INFORMATION

CLINICAL TRIALS

MICROBIOLOGY

NON-CLINICAL TOXICOLOGY AND PHARMACOLOGY

PATIENT MEDICATION INFORMATION