NOTIFICATION TO THE PRAC/EMA SECRETARIAT OF A REFERRAL UNDER ARTICLE 20 OF REGULATION (EC) 726/2004

E-mail: [redacted]

This notification is a referral under Article 20 of Regulation (EC) 726/2004 to the Pharmacovigilance Risk Assessment Committee (PRAC) made by the European Commission (EC):

Product(s) Name(s)	IXCHIQ
Active substance(s)	Chikungunya virus, strain CHIKV LR2006-OPY1, live attenuated
Pharmaceutical form(s)	All
Strength(s)	All
Route(s) of Administration	All
Marketing Authorisation Holder(s)	Valneva Austria GmbH

Background

IXCHIQ is a live attenuated chikungunya vaccine. It contains the live attenuated chikungunya virus (CHIKV) Δ5nsP3 strain of the ECSA/IOL genotype. IXCHIQ is a centrally authorised product approved in June 2024. It is indicated for active immunisation for the prevention of disease caused by chikungunya virus in individuals 12 years and older. IXCHIQ triggers a protective immune response against chikungunya virus in adults and adolescents that is maintained for at least 2 years after vaccination.

The safety profile of IXCHIQ was evaluated in around 4,000 individuals from clinical trials, including 350 older than 65 years. The most common side effects with IXCHIQ are headache, nausea, myalgia, arthralgia, fatigue, fever, vaccination site reactions (tenderness, pain, erythema, induration, swelling), white blood cell count decrease and liver function test increase. Chikungunya-like adverse reactions were reported in 12.1% of adult participants. The symptoms were mostly mild, but 1.8% of adult participants reported at least one severe symptom, most commonly fever or arthralgia. Longer-lasting symptoms (≥30 days) occurred in 0.4% of adult participants. Based on these data, sections 4.4 and 4.8 of the summary of product characteristics (SmPC) inform that IXCHIQ may cause severe or prolonged chikungunya-like adverse reactions. Like other live attenuated vaccines, IXCHIQ is contraindicated in immunodeficient or immunosuppressed patients due to a disease or treatment (section 4.3 of the SmPC).

Since January 2025, a large chikungunya outbreak has been affecting the European Union (EU) French overseas territories, prompting a vaccination campaign targeting individuals over 65 with comorbidities at risk of severe disease. The campaign was later expanded to include all individuals aged 18 and older. In the EU, there have been localised outbreaks in the past, however in 2025, no autochthonous cases of chikungunya disease have been reported in mainland EU. As of 25 April 2025, more than 44,000 chikungunya disease cases have been reported from the French overseas territories of Réunion, including at least 9 fatal cases[1].

Issues to be considered

Globally as of 30 April 2025, 15 cases of serious adverse events (SAEs) following vaccination with IXCHIQ have been reported by the marketing authorisation holder (MAH), including 9 from the EU (8 from France including La Reunion) and 6 from the United States of America (USA).

[1] https://www.santepubliquefrance.fr/recherche/#search=chikungunya

Of the 9 SAEs reported from the EU, 4 have occurred in people older than 80 years with multiple underlying comorbidities and who required hospitalisation. Two of these cases involved severe neurological complications in 84 years old individuals, which in one case led to death whilst the other patient is recovering in hospital. In both individuals, the vaccine strain of the chikungunya virus was detected in bodily fluids by polymerase chain reaction (PCR) test. As consequence, French public health authority (*Haute Autorité de Santé* [HAS]) recommended a temporary suspension of vaccinations for individuals over 65 until the necessary investigations are completed and called for a reassessment of the benefit/risk balance of IXCHIQ in subjects aged 65 and over, given the current uncertainties about the safety of this vaccine in this population[2].

In the USA, the 6 cases reported comprised neurological or cardiac SAEs following vaccination in travellers older than 67 years were reported (VAERS)[3]. Five of these individuals were hospitalised and all have recovered. All 6 people had a number of existing comorbidities. Although causality could not be determined, association of vaccination with the SAEs was assessed as plausible. For this reason, at their meeting on 16 April, the Advisory Committee on Immunization Practices (ACIP) of the United States (US) Centers for Disease Control and Prevention (CDC) recommended precaution when vaccinating people older than 65 years depending on the risk of exposure[4].

In view of the above, the EC initiates a procedure under Article 20 of Regulation (EC) No 726/2004 and requests the Agency to assess the above concerns and their impact on the benefit risk balance for the centrally authorised medicinal product IXCHIQ.

The EC requests the Agency to give its opinion by 30 September 2025 on whether the marketing authorisation for this product should be maintained, varied, suspended or revoked.

As the request comes from the evaluation of data resulting from pharmacovigilance activities, the opinion should be adopted by the Committee for Medicinal Products for Human Use (CHMP) on the basis of a recommendation of the PRAC.

In addition, the EC requests the Agency/PRAC to give its opinion, as soon as possible, as to whether temporary measures are necessary to ensure the safe and effective use of this medicinal product.

Signed Date: 5 May 2025
Olga Solomon
Head of Unit - Medicines: policy, authorisation and monitoring
Health and Food Safety Directorate General

2 Health authorities remove people aged 65 and over from the targets of the vaccination campaign against chikungunya with the IXCHIQ vaccine in Reunion Island and Mayotte - Ministry of Labour, Health, Solidarity and Families

3 Chikungunya Vaccine Information for Healthcare Providers | Chikungunya Virus | CDC

4 ACIP CHIKUNGUNYA VACCINES WORK GROUP ; ACIP Meeting Information | ACIP | CDC