08 May 2025
EMA/PRAC/158050/2025

PRAC List of questions

To be addressed by the marketing authorisation holder for IXCHIQ

Procedure under Article 20 of Regulation (EC) No 726/2004 resulting from pharmacovigilance data

IXCHIQ

EMA/REF/0000269473

Marketing authorisation holder: Valneva Austria GmbH

INN/active substance: Chikungunya vaccine (live)

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1. Questions

The marketing authorisation holder (MAH) is requested to address the following questions:

Question 1

The MAH is asked to provide the most recent figures on exposure to Ixchiq (administered doses) worldwide and by country, age category (12-17 years, 18-64 years, 65 years and older) and batches. Data on the use in clinical practice should be provided including information on vaccinee characteristics, concomitant treatments, co-administered vaccines and comorbidities. Exposure data in clinical studies should be presented by the MAH according to the same criteria.

Question 2

The MAH is requested to provide all available safety data relevant to evaluate the risk of serious adverse reactions with Ixchiq, accompanied by an analysis of such data. This should include all non-clinical data, clinical trial data (including both MAH-sponsored and non-MAH sponsored studies), pharmaco-epidemiological studies (including observational studies), and published literature.

In addition, the MAH is asked to provide a thorough cumulative review and causality assessment of all serious cases reported where Ixchiq is the suspected vaccine. Causality assessment should be performed for the serious cases using the WHO-UMC/AEFI scoring system and possible risk factors should be discussed. This evaluation should include the diagnostic certainty and case definitions (when available), as well as analyses on age and sex of the individual, relevant medical history, concomitant medications/vaccinations and illnesses, time to onset, outcome, seriousness criteria, possible chikungunya-like adverse reactions, and results of laboratory tests (e.g. for chikungunya and other infectious agents). It should be specified, for each case, which factors are known to be associated with immune dysfunction.

Potential clusters or similarities should be discussed, especially regarding vaccine batches, concomitant diseases, chikungunya-like adverse reactions, neurological, cardiovascular, or renal events.

Question 3

The MAH should discuss the possible mechanisms explaining the serious cases observed including viraemia kinetics of the vaccine virus, and impact of attenuation and vaccine batches used in the serious cases. It should also discuss whether age, pre-existing and concomitant conditions and concomitant medications are associated with a higher risk of serious adverse reactions, and if so, which.

Question 4

The MAH should discuss the rates of fatality, serious complications and long-term sequelae resulting from chikungunya for the age strata (12-17 years, 18-64 years, 65 years and older) in endemic areas to be put in perspective with the current figures of deaths and serious adverse reactions related to the vaccinal strain. This should include observed versus expected analyses for (i) fatal outcomes and (ii) encephalitis.

Same attempts should be made for travellers in endemic countries based on age strata.

Considering non-clinical and clinical data, the MAH should discuss the likelihood of serious cases in relation to age and comorbidities (known to be associated or not with immune alteration) outside the contraindication related to immunodeficiency/immunosuppression.

Question 5

The MAH is asked to provide a full benefit-risk balance assessment of Ixchiq depending on the age groups (12-17 years, 18-64 years, 65 years and older) for (i) people living in endemic areas, (ii) people living in areas of outbreak, (iii) travellers to endemic areas, and (iv) travellers to outbreak areas. This should include an assessment on the impact of occurrence of neurological, respectively visceral disease, on the benefit-risk balance, and consider how the benefit-risk balance may differ according to age and comorbidities.

Question 6

The MAH is asked to propose any risk minimisation measures which could be implemented to improve the benefit-risk balance of Ixchiq. Any proposed measures should be duly justified. In addition, the MAH should provide proposals to monitor the effectiveness of these risk minimisation measures. Communication activities (e.g. further DHPC) should also be discussed, as appropriate.

- In case of proposed changes to the SmPC/PL, the MAH is requested to provide the revised product information with the responses to this list of questions.

- In case materials for communication are considered needed, these should be provided as part of the responses to this list of questions.

- If any risk minimisation is proposed, the MAH should provide a revised risk management plan.