24 July 2025
EMADOC-1700519818-2313948

CHMP List of questions

To be addressed by the marketing authorisation holder for Tecovirimat SIGA

Procedure under Article 20 of Regulation (EC) No 726/2004

Tecovirimat SIGA

EMA/REF/0000287477

Marketing authorisation holder: SIGA Technologies Netherlands B.V.

INN/ active substance: tecovirimat

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1. Background

The marketing authorisation holder (MAH) is requested to address the below questions. Where the data available do not allow the MAH to fully address the question at the time of submission of the responses, a detailed justification should be provided accordingly, together with an estimate of the expected timelines, as to when additional data would be available and when it would be feasible for the MAH to fully address the question.

2. Questions

Question 1

The MAH should provide an overview of all clinical trials/expanded use programmes/registries including PALM007, STOMP, PLATINUM UK, PLATINIUM CANADA, UNITY, EPOXI trials, and any other relevant studies evaluating tecovirimat in the treatment of mpox, their current study status, populations enrolled and study objectives.

Question 2

The MAH should provide the marketing status and exposure to tecovirimat in the EEA, and worldwide. This should include data from completed and ongoing studies and all post-marketing sources.

Question 3

The MAH is requested to report all efficacy, viral load and pharmacokinetic data available from the above-mentioned studies (question 1), and from the literature. A particular focus should be placed on data from randomised controlled trials (RCT). The most updated available data should be provided.

A critical analysis and discussion of these data should be provided, including:

a. For RCTs, an analysis of the specifics of the trial setting, population (baseline and disease characteristics), inclusion/exclusion criteria and treatment conditions. These factors should be discussed in relation to the approved use in each of the therapeutic indications (that is, their relevance to the other indications apart from mpox should also be considered).

b. An analysis of the similarities/differences in the efficacy results for the different mpox (sub-) clades causing human infections, since authorisation of tecovirimat.

c. For RCTs, an analysis and discussion of the relation between (i) time from symptom onset to treatment initiation, and (ii) clinical efficacy.

d. Identification of other factors, if any, that may influence the efficacy of tecovirimat, including patient factors, disease factors, viral factors, concomitant medication/vaccination, other.

e. Discuss available evidence on an antiviral effect (or lack thereof) of tecovirimat.

Question 4

Please provide a summary of the preclinical efficacy data that were pivotal to the approval and generated since. Discuss reasons why these do not appear to be predictive of efficacy in all the human mpox studies.

Question 5

Please discuss the implications of the outcome of clinical studies in humans with mpox, with regards to anticipated efficacy against smallpox, cowpox and vaccinia infections.

Question 6

In relation to study PALM007, the MAH is further requested to:

a. Perform an exposure-response analysis with the patient data and discuss whether the efficacy PK target of 169 ng/mL predicts efficacy in humans.

b. Discuss the suitability of the population pharmacokinetic (popPK) model used, particularly in light of potential confounding factors (e.g. disease state, comorbidities, malnutrition status) and whether the model is fit-for-purpose to simulate plasma concentrations in the target population, given that covariates were not included.

c. Discuss whether the inclusion of data for the 50 mg and 100 mg dose/weight bands in the popPK model impacts the predictions of the model for the posology authorised in the EU, given the potential dosing inaccuracy at these dosage levels.

Question 7

The MAH is requested to report all safety data available from the above-mentioned studies (the most updated available data should be provided). A critical analysis and discussion of these data should be provided.

Question 8

Please provide a critical assessment of the overall impact of the above data on the benefit-risk balance of Tecovirimat SIGA in each of its authorised indications. This assessment should also include a discussion on whether there is a need for any amendments to the product information.