09 June 2017
EMA/PRAC/366034/2017

PRAC List of questions

To be addressed by the marketing authorisation holder

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

Procedure number: EMEA/H/A-20/1456/C/003862/0010

Invented name: Zinbryta

INN/active substance: daclizumab

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Questions to be addressed by 20 June 2017:

The marketing authorisation holders MAH are requested to address the following questions:

Question 1. The PRAC is to advise on the need for provisional measures, therefore, in the context of the current clinical use and considering the new data arising on the risk of liver injury, the MAH should make proposals for precautionary and provisional risk minimisation measures to be rapidly implemented (including, but not limited to, changes to conditions of the use of the product) or otherwise justify.

Questions to be addressed by 3 July 2017:

The marketing authorisation holders MAH are requested to address the following questions:

Question 1. The MAH should provide the following information on the use of daclizumab:

a) The current marketing status in the European Union and worldwide

b) The estimated patient exposure to daclizumab in the different EU Member States (number and patients years of treatment)

Question 2. The MAH should provide the following information on the MAH sponsored and not sponsored clinical studies with daclizumab:

a) Number of patients recruited and planned to be included in each completed and ongoing study (number of patients and time-exposure).

b) Characteristics of patients (e.g. age, gender, dose, duration of treatment).

c) Details about how the monitoring strategy for hepatic events is being carried out and whether case definitions for hepatic injury are implemented in CT.

Question 3. The MAH should provide detailed information on all cases (narrative and tabulated format) of liver injury, including cases from MAH-sponsored and non-MAH sponsored studies, spontaneous reports and literature. These should include time to onset (and time since last dose), management and outcome (including time to resolution when relevant), results of liver biopsies, number of doses received, patient characteristics, risk factors such as pre-existing liver disease, concomitant medications, results from biochemical liver parameters including liver enzymes, pattern of liver injury, treatment discontinuation due to increase of liver enzymes, and effect of dechallenge/rechallenge. For all the above cases, the MAH should include when available information on results and dates of monthly liver function monitoring.

Question 4. The MAH should provide calculation of the incidence (incidence rate and cumulative incidence) of liver enzyme elevations and serious liver injury in patients treated with daclizumab separated by clinical trials and post-marketing setting.

Question 5. In light of all the available data and taking into consideration the biological plausibility, the MAH should discuss the risk of liver injury associated with daclizumab and possible mechanisms for this adverse drug reaction.

Question 6. The MAH should discuss the effectiveness of current risk minimisation measures, regarding the risk of liver injury.

Question 7. The MAH should discuss the impact of the totality of the evidence on risk of liver injury on the benefit-risk of daclizumab in the current authorised indication.

Question 8. The MAH should provide proposals and justifications for any risk minimisation measures (including changes to the product information, DHPC and additional risk minimisation measure) which would improve the benefit/risk balance of daclizumab and how their effectiveness should be monitored.