7 January 2015
EMA/775397/2014
Executive Director

Letter of support for micro-aneurysm formation rate (MAFR) biomarker

On 07 June 2013 the applicant Critical Health S.A. requested qualification of micro-aneurysm formation rate (MAFR) measured with a validated automated method, as an enrichment biomarker for studies of clinically significant macular oedema (CSMO) pursuant to Article 57(1)(n) of Regulation (EC) 726/2004 of the European Parliament and of the Council.

During its meeting held on 01 – 04 September 2014, the SAWP agreed on the advice to be given to the applicant. During its meeting held on 22 - 25 September 2014, the CHMP adopted the advice to be given to the applicant.

The applicant proposes the micro-aneurysm formation rate (MAFR) measured with a validated automated method as a biomarker to enrich a clinical trial population to those at higher risk of developing clinically significant macular oedema (CSMO). MAFR as calculated by a validated automated method seems as a very promising biomarker for enriching a patient population at higher risk for the development of CSMO. It seems to be a complement to other markers (e.g. metabolic control) for the risk of progression of DR as an additive value is indicated. The restriction to a target population of subjects with type 2 diabetes and ETDRS DR severity grades 20 to 35, i.e. mild to moderate DR may also be reasonable. The MAFR as calculated by a validated method also has the advantages of allowing a rapid, objective and automated evaluation of the MAFR which is an important advantage, especially in the conduct of large clinical trials. However, to proceed to a qualification opinion, additional data are needed.

In a clinical trial of interventions aiming to prevent development of CSMO in subjects in earlier stages of diabetic retinopathy (DR), event rates are sparse during the relatively short duration of an interventional trial. The rate of progression is also highly variable between subjects. There is currently no comprehensive risk calculator to identify patients who are at an increased risk for the development of CSMO within a reasonable time frame. EMA agrees that there is a need to identify biomarkers that predict development of CSMO to facilitate the design of clinical trials of a aiming to intervene in early stages of DR. The biomarker letter of support is issued on the basis of this qualification advice.

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Sincerely,

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