Opening statement

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Infarmed

EMRN workshop on Geographic Atrophy endpoints – 29 April 2026

Disclaimers

No conflict of interests

Outline

- **Context**; Framework for drug approval
- **Regulatory expectations for**
  - Primary Endpoints for Efficacy in Pivotal Trials in general
  - Using a new clinical functional endpoint

Later today there will be a presentation on
Regulatory Expectations for **new surrogate** endpoints - efficacy

Framework: legal and scientific - medicines for human use

AI generated image

Efficacy Endpoints principles 1

The primary efficacy endpoint for the pivotal trials for the Marketing authorization (MA) should

A. be **clinically relevant** and reflect disease burden in the target population

A. OR

B. be of **adequate surrogacy** for predicting disease burden or sequelae.(E8 R1)

Scenario A
Primary clinical (functional) efficacy endpoint

Regulatory expectations at MAA:

Applicants have understood and evidenced **the capability** – *the measurement properties*- of the endpoint to provide **convincing evidence** on benefit:

Have pre-defined the primary endpoint **details** in the pivotal study protocol/statistical analysis plan, including clinically relevant effect sizes

Recommended regulatory interactions in Scientific advice and qualification for novel endpoints

Endpoint data:

Exploratory and Confirmatory data

Scientific literature

Scenario A
Primary **clinical (functional)** efficacy endpoint

Regulatory expectations at MAA

Applicants need to explain the **clinical relevance** of the endpoint for the target population/context.

- Justify the proposed ***concept*** measured; and that this is a ***clinical efficacy*** endpoint [and not just a surrogate for efficacy]
- Justify and explain the **minimally clinical important difference** (MCID)
- Pivotal evidence of benefits is expected to show a clinically meaningful difference, and not just statistical significance

Geographic Atrophy (GA) primary endpoint

What are the concerns about the current anatomical endpoints, e.g. slowing GA lesion progression?

Concerns:

- Anatomical / imaging endpoints are surrogate endpoints
    - Surrogate endpoints are used in trials as a substitute of the treatment effects of an intervention on the target outcome(s) of ultimate clinical interest, events measuring how patients feel, function, or survive.
- Does not yield a measure of clinical benefit that can be weighed directly against adverse effects
- Might not be a true predictor of benefit of treatment
- CHMP needs to understand when and to what extent a certain lesion size reduction would turn into perceivable patient benefit with treatment.

Objective of GA workshop

- to focus on how potential endpoints can meet these regulatory requirements going forward in pivotal clinical trials of treatments for geographic atrophy
- So that at MAA, CHMP can understand clearly any benefits of a proposed new treatment, and thus be able weigh this in relation to the risks
- We will focus on the overall questions
    - What functional endpoints are *currently* best suited for this purpose?
    - What functional endpoints are emerging and what gaps remain / how can they be filled
    - What is the status of the surrogate endpoints and what gaps remain / how can they be filled
- All this - in order to facilitate medicinal product development for GA, and thus address the unmet need for many EU patients with GA.

Regulatory caveats

- As regulators we will take any new information back under consideration;
- We will not discuss individual procedures, not re-open the recent CHMP discussions, nor disclose any confidential information.
- We can give regulators' views where we have had CHMP opinions on specific issues, otherwise any views will be personal opinions.
- In the wrap up at the end of the meeting, we will layout the next steps and outcomes
- We very much look forward to hearing the state of art from the research, clinical and patient community

Thank you

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