EDA Assessment Report for Biological Medicinal Product

(Scientific Discussion)

Vabysmo

Date: July 2024

Assessment report

Unit: Technical Assessment Unit

Vabysmo

Administrative information:

Trade name of the medicinal product:	Vabysmo
INN (or common name) of the active substance(s):	Faricimab
Manufacturer of the finished product	F. Hoffmann-La Roche AG, Wurmisweg, 4303 Kaiseraugst - SWITZERLAND
Marketing Authorization holder	Roche Registration GmbH, Emil-Barell-Strasse 1, Grenzach-Wyhlen, 79639 - GERMANY;
Applied Indication(s):	-treatment of neovascular (wet) age related macular degeneration (nAMD) -treatment of diabetic macular edema (DME)
Pharmaceutical form(s) and strength(s):	solution for Injection -Strength: 120 mg/ ml
Route of administration	Intravitreal Injection
Approved pack	Carton folding box consists of: one colorless Borosilicate (type I) glass vial with fluororesin laminated butyl grey rubber stopper and aluminum seal with plastic flip off cap. Co-packaged with a stainless-steel transfer filter needle and inner leaflet.

List of abbreviations

Ang-2	angiopoetin-2
CHO	Chinese hamster ovary
DME	diabetic macular edema
DP	Drug product
EMA	European medicines agency
FDA	Food and Drug Administration
GMP	Good manufacturing practice
DS	Drug substance

nAMD	Neovascular age-related macular
VEGF	vascular endothelial growth factor
VEGF-A	vascular endothelial growth factor-A

Dossier initial submission and evaluation process.

- The product was submitted for registration via reliance level 1 (EMA and FDA approved)
- The dossier evaluation by the registration administration units was started on 11.12.2022 after providing all the required documents according to the "Checklist for documents of new biological products registration file" along with other supportive documents (EMA list of questions and answers).

1. **'General introduction about the product including brief description of the AI, its mode of action and indications:**

-The active substance (faricimab) is a recombinant bispecific antibody produced in Chinese hamster ovary (CHO) cells and consists of two different heavy chains (452 amino acid residues and 462 amino acid residues) and two different light chains (214 amino acid residues and 213 amino acid residues) with inter- and intra-chain disulfide bonds, that are typical for IgG1 antibodies plus an additional disulfide bridge in the CH3-CH3 interface.
-Faricimab is a next generation antibody with a dual action that targets not one but two pathways involved in angiogenesis/vascularisation/inflammation and retinal vessel destabilisation in the eye. Faricimab selectively binds with high affinity to VEGF-A and Ang-2 thereby preventing binding of VEGF-A and Ang-2 to its receptors. Binding of VEGF-A and Ang-2 to their receptors results in retinal vessel destabilization, inflammation, endothelial cell proliferation, neovascularisation and vascular leakage, which mediate onset and progression of neovascular form of age-related macular degeneration (nAMD), diabetic retinopathy and diabetic macular oedema (DME). The mechanism of action of faricimab works through the interference with the ligand-receptor binding process in Ang-2 and VEGF pathways that play a key role in these retinal diseases.
- The finished product is presented as a solution for injection containing 120 mg/ml of faricimab as active substance. Each vial contains 28.8 mg faricimab in 0.24 mL solution. This provides a usable amount to deliver a single dose of 0.05 mL solution containing 6 mg of faricimab.
The container closure system consists of a Type I glass vial with a fluororesin-laminated butyl rubber stopper and crimped with an aluminum seal fitted with a plastic flip-off cap.
- Vabysmo is a medicine used to treat adults with:
• the 'wet' form of age-related macular degeneration (AMD), a disease that affects the central part of the retina (called the macula) at the back of the eye. The wet form of AMD is

caused by abnormal growth of blood vessels beneath the retina which may leak fluid and blood and cause swelling;
• impaired vision due to macular oedema caused by diabetes.

The macula provides central vision that is needed to see details for everyday tasks such as driving, reading and recognizing faces. The diseases cause the gradual loss of the central part of a person's vision.

2. **Quality aspects:**

- **Manufacturer(s):**

Drug substance:
- The Active substance is manufactured at Roche Diagnostics GmbH, Nonnenwald 2, Penzberg 82377 - GERMANY

Drug product:
- The Finished product are manufactured at F. Hoffmann-La Roche AG Wurmisweg 4303 Kaiseraugst -Switzerland

Manufacturing of both DS and DP are performed in accordance with GMP regulations.

- **Stability**

Drug substance:
- **Approved Shelf Life: 36 months**
- **Approved storage Conditions:**
  - **Store at -40°C (- 30°C to - 50°C)**

Drug product:
- **approved Shelf Life: 30 Months**
- **approved Storage Conditions:**
  - Store in a refrigerator **(2-8** ◦C**).**
  - Do not freeze
  - Do not shake
  - Keep the vial in the outer carton in order to protect from light.

- Prior to use, the unopened vial may be kept at room temp, 20◦C to 25◦C, for up to 24 hrs.

Ensure that the injection is given immediately after preparation of the dose.

3. Non-clinical and clinical aspects:

-The nonclinical data indicate that faricimab has the potential to be a safe and efficacious therapeutic agent for the treatment neovascular (wet) age related macular degeneration (nAMD)

-In conclusion the overall benefit/risk of Vabysmo is favorable in the following indication(s):

• neovascular (wet) age-related macular degeneration (nAMD),
• visual impairment due to diabetic macular oedema (DME).

➢ **General Conclusion and Recommendations if any:**

Based on the review of CTD modules and other supplementary documents, the product is approved.

For more information, please visit EMA published assessment report link:

https://www.ema.europa.eu/en/documents/assessment-report/vabysmo-epar-public-assessment-report_en.pdf