Vabysmo (faricimab-svoa)

New Product Slideshow

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Introduction

- **Brand name:** Vabysmo
- **Generic name:** Faricimab-svoa
- **Pharmacologic class:** Vascular endothelial growth factor (VEGF) inhibitor/angiopoietin-2 (Ang-2) inhibitor
- **Strength and Formulation:** 120mg/mL; solution for intravitreal injection; preservative-free
- **Manufacturer:** Genentech, Inc.
- **How supplied:** Single-dose vial—1 (w. needle)
- **Legal Classification:** Rx

Indications

- Treatment of patients with:
  - Neovascular (wet) age-related macular degeneration (nAMD)
  - Diabetic macular edema (DME)

Dosage and Administration

- Administered via **intravitreal injection** by a qualified physician under aseptic conditions.
- Each vial and syringe should only be used to treat a single eye.
- Adequate anesthesia and a broad spectrum microbicide should be administered prior to the injection.

Dosage and Administration - nAMD

- **Neovascular (wet) age-related macular degeneration (nAMD)**
  - Inject 6mg (0.05mL of 120mg/mL solution) once every 4 weeks (approx. every 28±7 days, monthly) for the 1st 4 doses, followed by optical coherence tomography and visual acuity evaluations 8 and 12 weeks later to inform whether to give a 6mg dose on one of the following 3 regimens:
    - (1) weeks 28 and 44;
    - (2) weeks 24, 36 and 48; or
    - (3) weeks 20, 28, 36 and 44.
  - Although additional efficacy was not demonstrated in most patients when Vabysmo was dosed every 4 weeks compared with every 8 weeks, some patients may need every 4 week dosing after the first 4 doses.
  - Assess patients regularly.

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Dosage and Administration - DME

- **Diabetic macular edema (DME)**
  - **Regimen 1**: Inject 6mg (0.05mL of 120mg/mL solution) once every 4 weeks (approx. every 28±7 days, monthly) for at least 4 doses.
  - If after at least 4 doses, resolution of edema is achieved based on the central subfield thickness (CST) of the macula as measured by optical coherence tomography, then the dosing interval may be modified by extensions of up to 4 week interval increments or reductions of up to 8 week interval increments based on CST and visual acuity evaluations through week 52; or **Regimen 2**: 6mg once every 4 weeks for the 1st 6 doses, followed by 6mg every 8 weeks over the next 28 weeks.
  - Although additional efficacy was not demonstrated in most patients when Vabysmo was dosed every 4 weeks compared with every 8 weeks, some patients may need every 4 week dosing after the first 4 doses.
  - Assess patients regularly.

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Considerations for Specific Populations

- **Pregnancy:** No adequate and well-controlled studies in pregnant women; should not be used unless the potential benefit outweighs the potential risk to the fetus.
- **Nursing mothers:** No information on the presence of faricimab in human milk; consider benefits of breastfeeding along with mother's clinical need and potential adverse effects.
- **Females of reproductive potential:** Use effective contraception prior to the initial dose, during, and for at least 3 months after the last dose.
- **Pediatric**: Not established.
- **Geriatrics**: No significant differences in efficacy or safety of faricimab were seen with increasing age. No dosage adjustment is required in patients aged ≥65yrs.

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Contraindications

- Ocular or periocular infection.
- Active intraocular inflammation.
- Known hypersensitivity to faricimab or any of the excipients in Vabysmo.

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Warnings and Precautions

- Instruct patients to report any symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management.
- Transient increases in intraocular pressure (IOP) were observed within 60 minutes of intravitreal injection, including with Vabysmo; monitor IOP and the perfusion of the optic nerve head.
- Potential risk of arterial thromboembolic events following intravitreal use of VEGF inhibitors (eg, nonfatal stroke or MI, vascular death).

Adverse Reactions

- **Most common** (≥5%): Conjunctival hemorrhage.
- **Others**: Vitreous floaters, increased IOP, eye pain, intraocular inflammation, eye irritation, ocular discomfort, vitreous hemorrhage, retinal pigment epithelial tear (nAMD only).

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Mechanism of Action

- **Faricimab** is a humanized bispecific antibody that acts through inhibition of 2 pathways by binding to VEGF-A and Ang-2.
- By inhibiting VEGF-A, faricimab suppresses endothelial cell proliferation, neovascularization and vascular permeability.
- By inhibiting Ang-2, faricimab is thought to promote vascular stability and desensitize blood vessels to the effects of VEGF-A.
  - The contribution of Ang-2 inhibition to the treatment effect and clinical response for nAMD and DME has yet to be established.

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Clinical Trials - nAMD

- Approval for nAMD was based on 2 randomized, multicenter, double-masked, active comparator-controlled, 2-year phase 3 studies (**TENAYA** [ClinicalTrials.gov Identifier: NCT03823287], and **LUCERNE** [ClinicalTrials.gov Identifier: NCT03823300]).
- The studies included a total of 1329 newly diagnosed, treatment-naïve patients.
- Patient ages ranged from 50 to 99 with a mean of 75.9 years.

Clinical Trials - nAMD

- Patients were randomly assigned 1:1 to receive either:
  - Aflibercept 2mg administered fixed every 8 weeks after 3 initial monthly doses; or
  - Vabysmo 6mg administered every 4 weeks for the first 4 doses, followed by optical coherence tomography and visual acuity evaluations 8 and 12 weeks later to determine whether to give a 6mg dose on one of the following 3 regimens: 1) weeks 28 and 44 (also referred to as Q16W dosing); 2) weeks 24, 36 and 48 (also referred to as Q12W dosing); or 3) weeks 20, 28, 36 and 44 (also referred to as Q8W dosing).
- The **primary endpoint** for both studies was the average change from baseline in Best Corrected Visual Acuity (BCVA) when averaged over the week 40, 44, and 48 visits and measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) letter chart.

Clinical Trials - nAMD

- **At week 48**, after 4 initial monthly doses in the Vabysmo arm:
  - 45% received the weeks 28 and 44 dosing
  - 33% received the weeks 24, 36, and 48 dosing
  - 22% received dosing every 8 weeks
- Study findings showed that patients did well on 2 doses spaced 16 weeks apart or on 3 doses spaced every 12 weeks apart.
- The percentages, however, may not be generalizable to a broader nAMD population.
- The inclusion/exclusion criteria limited enrollment to a select subset of treatment naïve, newly diagnosed nAMD patients.

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Clinical Trials - nAMD

- In both studies, Vabysmo treated patients had a noninferior mean change from baseline in BCVA compared with patients treated with aflibercept.

	TENAYA		LUCERNE	
	Vabysmo N=334	Aflibercept N=337	Vabysmo N=331	Aflibercept N=327
Mean change in BCVA (95% CI)	5.8 (4.6-7.1)	5.1 (3.9-6.4)	6.6 (5.3-7.8)	6.6 (5.3-7.8)
Difference in LS mean (95% CI)	0.7 (-1.1, 2.5)		0.0 (-1.7, 1.8)	

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Clinical Trials - DME

- Approval for DME was based on 2 randomized, multicenter, double-masked, active comparator-controlled, 2-year phase 3 studies (**YOSEMITE** [ClinicalTrials.gov Identifier: NCT03622580], and **RHINE** [ClinicalTrials.gov Identifier: NCT03622593]), which included a total of 1891 diabetic patients.
- Patient ages ranged from 24 to 91 with a mean of 62.2 years.
- The overall population included anti-VEGF naive patients (78%) and patients who had been previously treated with a VEGF inhibitor prior to study participation (22%).

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Clinical Trials - DME

- Patients were randomly assigned 1:1:1 to receive either:
  - Aflibercept 2mg administered fixed every 8 weeks after the first 5 monthly doses;
  - Vabysmo 6mg every 8 weeks after the first 6 monthly doses (referred to as Vabysmo Q8W); or
  - Vabysmo 6mg every 4 weeks for at least 4 doses and until the CST of the macula was less than approx. 325 microns, then the dosing interval was modified by up to 4 week interval extensions or reductions in up to 8 week interval increments based on CST and visual acuity disease activity criteria at study dosing visits (referred to as Vabysmo Variable).
- The **primary endpoint** for both studies was the average change from baseline in BCVA at year 1 (average of the week 48, 52, and 56 visits), measured by the ETDRS Letter Score.

Clinical Trials - DME

- After 4 initial monthly doses, patients in the Vabysmo Variable arm could have received between the minimum of 3 and the maximum of 11 total injections through week 56 inclusive.
- **At week 56**:
  - 32% of patients had completed at least 1 Q12W interval followed by 1 full Q16W interval.
  - 17% were treated on Q8W and/or Q4W dosing intervals.
  - 7% were only on Q4W.
- Sustainability of the Q16W dosing interval could not be determined based on 1 year data alone.
- Percentages reflect what happened in the studies and are not generalizable to the broader DME population.

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Clinical Trials - DME

- In both studies, Vabysmo Q8W and Vabysmo Variable treated patients had a mean change from baseline in BCVA that was noninferior to the patients treated with aflibercept Q8W.

	YOSEMITE			RHINE		
	Vabysmo Q8W N=315	Vabysmo Variable N=313	Aflibercept Q8W N=312	Vabysmo Q8W N=317	Vabysmo Variable N=319	Aflibercept Q8W N=315
Mean change in BCVA (97.5% CI)	10.7 (9.4-12.0)	11.6 (10.3-12.9)	10.9 (9.6-12.2)	11.8 (10.6-13.0)	10.8 (9.6-11.9)	10.3 (9.1-11.4)
Difference in LS mean (97.5% CI)	-0.2 (-2.0, 1.6)	0.7 (-1.1, 2.5)		1.5 (-0.1, 3.2)	0.5 (-1.1, 2.1)	

Clinical Trials – nAMD & DME

- For all nAMD and DME studies, treatment effects in evaluable subgroups (eg, by age, gender, race, baseline visual acuity) were generally consistent with the results in the overall population.
- For the DME studies, treatment effects in the subgroup of patients who were anti-VEGF naïve prior to study participation were similar to those observed in the overall population.

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/vabysmo/