VABYSMO™

faricimab-svoa injection 6 mg

ACCESS VABYSMO WITH CONFIDENCE

A quick start guide to coverage and reimbursement for practices

Flexible 1-4 month dosing in nAMD and DME, and monthly dosing for 6 months in RVO

Please see Important Safety Information in the full VABYSMO Prescribing Information.

Genentech

A Member of the Roche Group

Start Now With Dual-Pathway VABYSMO

Genentech helps your patients begin and continue to access VABYSMO with our robust patient support services

Coverage and reimbursement support:
Genentech Ophthalmology Access Solutions

Financial assistance for eligible patients:
Affordability Options

Free medicine for eligible patients:
Genentech Patient Foundation

BUSINESS CARD HERE

Our dedicated team is ready to help.

Contact your Field Reimbursement Manager to get started.

Connecting Patients to VABYSMO

Enrolling in coverage, reimbursement and financial assistance services for VABYSMO requires 2 simple forms.

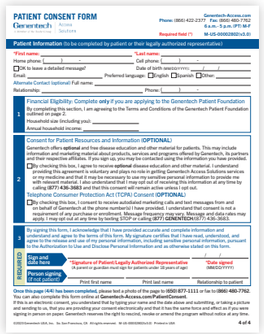
Prescriber Service Form


Genentech
SUBMIT ONLY REQUESTED DOCUMENTS
Prescriber Service Form
Required field (*)
Step 1 Patient Information
Step 2 Insurance Information
Step 3 Patient's Therapy (Check all that apply)
Step 4 Diagnosis and Clinical Information

Where to find
Genentech-Access.com/VABYSMO

How to submit
- Quick Enroll
- My Patient Solutions for Health Care Practices
- Fax to (866) 724-9412

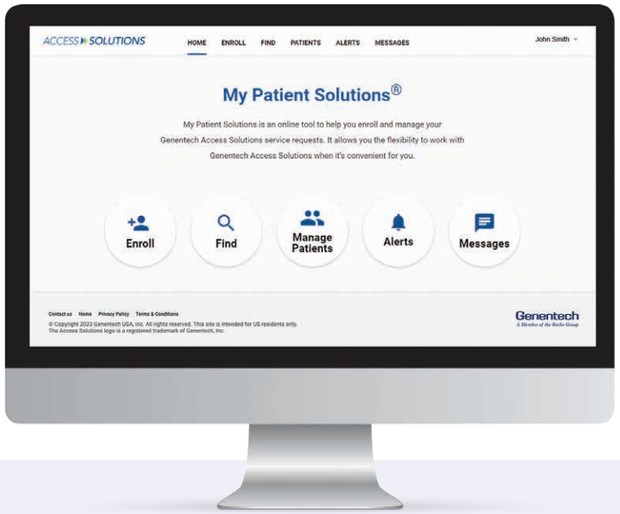
Patient Consent Form


PATIENT CONSENT FORM
Genentech Access Solutions
Genentech-Access.com
Phone: (866) 422-2377 Fax: (650) 467-7762
M-US-00006892v3.01
Patient Information (to be completed by patient or their legally authorized representative)
1 Financial Eligibility: Complete only if you are applying to the Genentech Patient Foundation
2 Consent for Patient Resources and Information (OPTIONAL)
Telephone Consumer Protection Act (TCPA) Consent (OPTIONAL)
3 By signing this form I acknowledge that the information provided is accurate and complete to the best of my knowledge and agree to the terms of this form. My signature confirms that I have read, understood, and agree to the release and use of my personal information, including sensitive personal information, pursuant to the Authorization to Use and Disclose Personal Information and as otherwise stated on this form.
REQUIRED
Sign and date here
*Signature of Patient/Legally Authorized Representative
*Date signed (MM/DD/YYYY)
Person signing if not patient
Print first name
Print last name
Relationship to patient
Once this page (4/4) has been completed, please text a photo of the page to (650) 877-1111 or fax to (866) 480-7762.
You can also complete this form online at Genentech-Access.com/PatientConsent.
If this is an electronic consent, you understand that by typing your name and the date above and submitting, or taking a picture and sending to us, that you are providing your consent electronically and that it has the same force and effect as if you were signing in person or paper. Genentech reserves the right to rescind, revoke or amend the program without notice at any time.
4 of 4

Where to find
Genentech-Access.com/PatientConsent

How to submit
- eSubmit
- My Patient Solutions
- Take a photo and text it to (650) 877-1111
- Fax to (866) 480-7762

My Patient Solutions® for Health Care Practices:
The flexibility to work with us when it's convenient for you



Features include:

- Message a Genentech Ophthalmology Access Solutions Specialist
- Co-pay assistance referrals
- Paperless enrollment and re-enrollment
- Benefits Investigation Reports
- Service request details
- Prior authorization follow-ups
- Genentech Patient Foundation eligibility and shipment coordination
- Benefits reverifications
- Simultaneous account registration

Be sure to submit these forms together **for fast and efficient processing**.

Register for an account or log in at **Genentech-Access.com/MPS**.

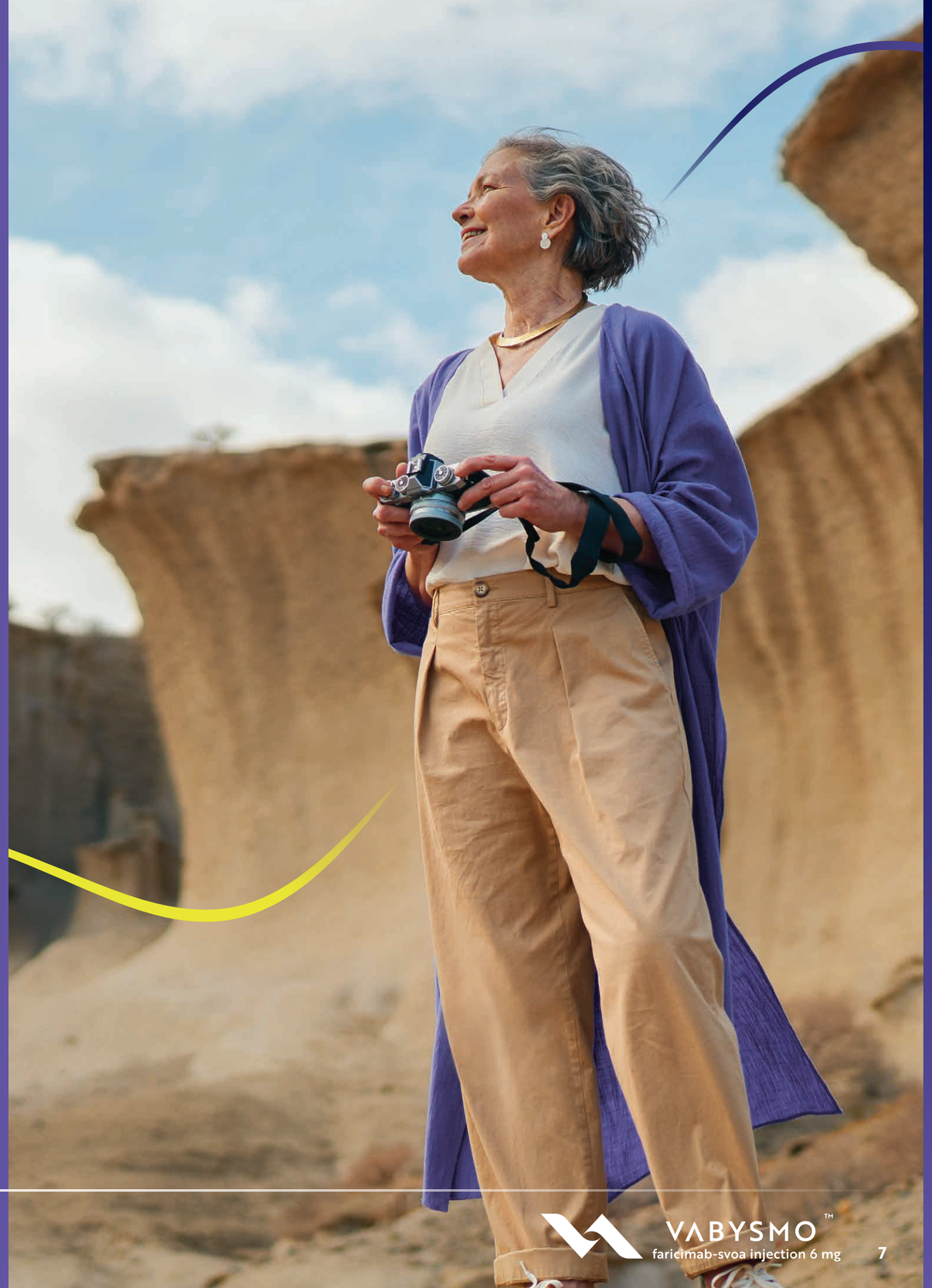
Genentech Ophthalmology Access Solutions Support for Patients Prescribed VABYSMO

Our dedicated Genentech team supports your practice throughout the coverage and reimbursement process. We provide:

- Benefits investigations
- Resources for prior authorizations (PAs)
  Including sample letters and required forms
- Resources for denials and appeals
  Including sample letters and specific appeal requirements
- Information about authorized specialty distributors
- Referrals to financial assistance options
- Sample billing and coding information
- Benefits reverification support

For more information, please visit **VABYSMO.com/support**.

The completion and submission of coverage- or reimbursement-related documentation are the responsibility of the patient and health care provider. Genentech makes no representation or guarantee concerning coverage or reimbursement for any service or item.



Benefits Reverification Support From Genentech Ophthalmology Access Solutions

Considerations for reverifications include:

IDENTIFY which patients require reverifications

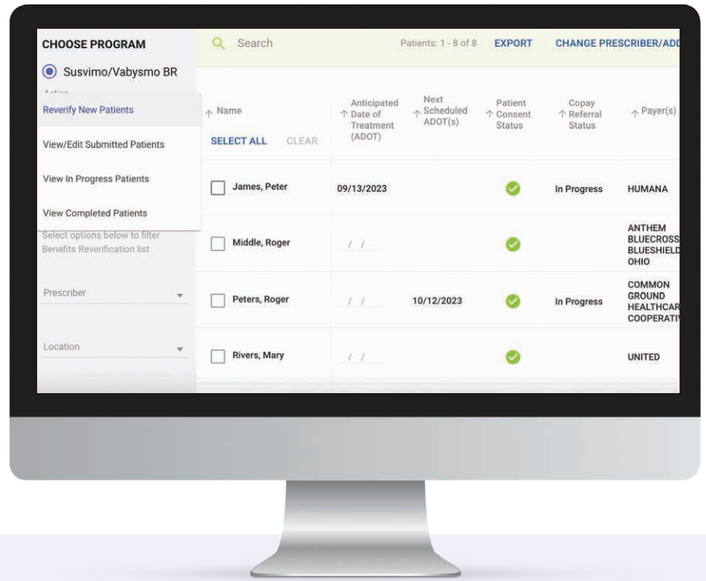
DOCUMENT any PA numbers and expiration dates

GATHER required forms and documents

WORK within the required timing to avoid treatment delays

Benefits reverifications are available on a rolling basis via **My Patient Solutions**.

Benefits reverification using My Patient Solutions® for Health Care Practices



You can use My Patient Solutions to:

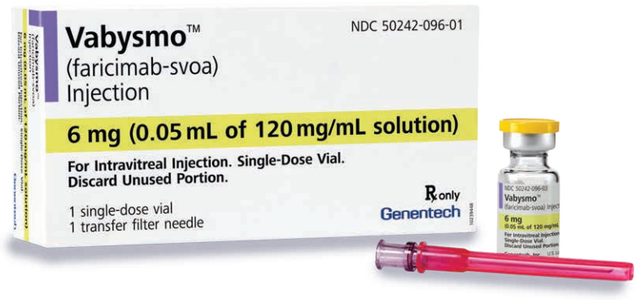
- Request reverifications for multiple patients at once
- Manage your patient list
- Update a patient's insurance information
- Check the status of any expiring Patient Consent Forms and directly upload a new form
- View or change your patient's anticipated treatment date

Please see Important Safety Information in the full VABYSMO Prescribing Information.

How to Acquire VABYSMO

VABYSMO is available to order as a single-dose vial and as a prefilled syringe (PFS).

Single-Dose Vial



PFS

For the latest list of authorized specialty distributors visit **Genentech-Access.com/VABYSMO**.

Genentech does not influence or advocate the use of any one specialty distributor. We make no representation or guarantee of service or coverage of any item.

Replacing spoiled medicine

To submit a request for replacement of spoiled product or to obtain additional information about the Genentech Spoilage Replacement Program:

- Visit **gene.com/customerservice** and select returns
- Call the Genentech Ophthalmology Support Line at **(833) EYE-GENE**/(833) 393-4363 and press 2

VABYSMO Sampling Program

If you are interested in requesting VABYSMO samples, **contact your Therapeutic Area Manager (TAM)**.

Specialty distributors for VABYSMO

Besse Medical
(800) 543-2111
besse.com

Cardinal Health Puerto Rico
(787) 625-4200
orderexpress.cardinalhealth.com

Cardinal Health Specialty
(866) 677-4844
specialtyonline.cardinalhealth.com

CuraScript SD
(877) 599-7748
curascriptsd.com

McKesson Plasma and Biologics
(877) 625-2566
connect.mckesson.com

McKesson Specialty Health
(855) 477-9800
mscs.mckesson.com

Metro Medical
(800) 768-2002
metromedicalorder.com

Drug and Administration Codes for VABYSMO

NDC Codes

Package*	Code		Description
	10-digit	**11-digit**	
Carton (vial)	50242-096-01	50242-0096-01	VABYSMO (6 mg [0.05 mL of 120 mg/mL solution]) in a single-dose vial with sterile 5-micron, blunt transfer filter needle (18-gauge × 1½-inch)
Vial	50242-096-03	50242-0096-03	VABYSMO (6 mg [0.05 mL of 120 mg/mL solution]) in a single-dose vial
Prefilled Syringe (PFS)	50242-096-06	50242-0096-06	VABYSMO (6 mg [0.05 mL of 120 mg/mL solution]) in a single-dose prefilled syringe with a sterile injection filter needle (30-gauge × ½-inch, Extra Thin Wall)

HCPCS Codes

Type	Code	Description
HCPCS code	J2777	Injection, faricimab-svoa, 0.1 mg
HCPCS: Modifier†	JZ	Zero drug amount discarded/not administered to any patient

Bill 60 units with J2777 for the 6-mg single-dose of VABYSMO. Payers might have different preferences for billing for VABYSMO. Check with your local payers for specific billing unit information.

Administration Codes

Type	Code	Description
CPT code	67028	Intravitreal injection of a pharmacologic agent (separate procedure)
CPT modifier	-LT	Left eye modifier
	-RT	Right eye modifier

The latest sample codes, including ICD-10-CM diagnosis codes for nAMD, DME and RVO, are available at **VABYSMO.com/support**.

CPT=Current Procedural Terminology; DME=diabetic macular edema; HCPCS=Healthcare Common Procedure Coding System; ICD-10-CM=International Classification of Diseases, 10th Edition, Clinical Modification; nAMD=neovascular (wet) age-related macular degeneration; NDC=National Drug Code; RVO=macular edema following retinal vein occlusion.

*Some payers may require the vial NDC instead of the carton. Please check the individual payer's NDC billing policy for billing direction.

†Beginning July 1, 2023, CMS requires the use of the JZ modifier to indicate there were no units of a drug discarded.

Drug and Administration Co-pay Assistance From the Genentech Ophthalmology Co-pay Program

Eligible commercially insured patients pay as little as:

$0
per drug co-pay, up to $15,000 per calendar year

$0
per administration co-pay, up to $1,000 per calendar year

For more information or to get started:

- **Scan** or **click** this QR code to visit EyeOnCopay.com
- **Call** (855) 218-5307 from 9 a.m. to 8 p.m. ET, Monday–Friday
- **Enroll** patients directly using the Prescriber Service Form and Patient Consent Form

The Product and Administration Co-pay Programs ("Programs") are valid ONLY for patients with commercial (private or non-governmental) insurance who have a valid prescription for a Food and Drug Administration (FDA)-approved indication of a Genentech medicine. Patients using Medicare, Medicaid or any other federal or state government program (collectively, "Government Programs") to pay for their Genentech medicine and/or administration services are not eligible.

Under the Programs, the patient may be required to pay a co-pay for drug costs and a co-pay for administration costs. The final amount owed by a patient may be as little as $0 for the Genentech medicine or administration of the Genentech medicine (see Program specific details available at the Program website). The total patient out-of-pocket cost is dependent on the patient's health insurance plan. The Programs assist with the cost of the Genentech medicine and the Genentech medicine administration only. It does not assist with the cost of other administrations, medicines, procedures or office visit fees. After reaching the maximum Programs' benefit amounts, the patient will be responsible for all remaining out-of-pocket expenses. The amount of the Programs' benefits cannot exceed the patient's out-of-pocket expenses for the cost of the Genentech medicine or administration fees for the Genentech medicine.

All participants are responsible for reporting the receipt of all Programs' benefits as required by any insurer or by law. The Programs are only valid in the United States and U.S. Territories and are void where prohibited by law. The Drug Co-pay Program shall follow state restrictions in relation to AB-rated generic equivalents (e.g., MA, CA) where applicable. The Administration Co-pay Program is not valid for Massachusetts or Rhode Island residents. No party may seek reimbursement for all or any part of the benefit received through the Programs. The value of the Programs is intended exclusively for the benefit of the patient. The funds made available through the Programs may only be used to reduce the out-of-pocket costs for the patient enrolled in the Programs. The Programs are not intended for the benefit of third parties, including without limitation third party payers, pharmacy benefit managers, or their agents. If Genentech determines that a third party has implemented programs that adjust patient cost-sharing obligations based on the availability of support under the Programs and/or excludes the assistance provided under the Programs from counting towards the patient's deductible or out-of-pocket cost limitations, Genentech may impose a per fill cap on the cost-sharing assistance available under the Programs. Submission of true and accurate information is a requirement for eligibility and Genentech reserves the right to disqualify patients who do not comply from Genentech programs. Genentech reserves the right to rescind, revoke or amend the Programs without notice at any time.

Additional terms and conditions apply. Please visit the co-pay Program website for the full list of Terms and Conditions.

Referrals to Independent Co-pay Assistance Foundations

For patients who are not able to use the Genentech Ophthalmology Co-pay Program, including those with Medicare or Medicaid, Genentech Ophthalmology Access Solutions offers referrals to independent co-pay assistance foundations.

For more information or to get started:

- **Call** (866) 724-9394 from 9 a.m. to 8 p.m. ET, Monday–Friday
- **Scan** this QR code for a list of independent co-pay assistance foundations

Independent co-pay assistance foundations have their own rules for eligibility. Genentech has no involvement or influence in independent foundation decision-making or eligibility criteria and does not know if a foundation will be able to help your patient. We can only refer your patient to a foundation that supports their disease state. Genentech does not endorse or show preference for any particular foundation. The foundations to which we refer your patient may not be the only ones that might be able to help.

Free VABYSMO for Eligible Patients From the Genentech Patient Foundation

Is My Patient Eligible?

Genentech Patient Foundation eligibility depends on your patients' health insurance and financial situation. They may qualify if they are in 1 of the 3 groups below.

1. "I have **no insurance**."

For a household of 1 to 4 people, total yearly income is under $150,000.

- For households with more than 4 people, add $25,000 to the yearly income limit for each additional person

2. "I **have insurance**, but it doesn't cover my Genentech medicine."

3. "I **have insurance** that covers my Genentech medicine, but the out-of-pocket maximum set by my health insurance plan is more than 7.5% of my yearly income."

Household size	Yearly income
1 person	Under $75,000
2 people	Under $100,000
3 people	Under $125,000
4 people	Under $150,000

For households with more than 4 people, add $25,000 to the yearly income limit for each additional person.

Not sure if your patient is eligible?

- Call **(888) 941-3331** to speak with a live Foundation Specialist
  – We offer support in many different languages
- Visit **GenentechPatientFoundation.com** for more information

Genentech reserves the right to modify or discontinue the program at any time and to verify the accuracy of information submitted.

Genentech
A Member of the Roche Group
Patient Foundation

Indications and Important Safety Information

INDICATIONS

VABYSMO (faricimab-svoa) is a vascular endothelial growth factor (VEGF) inhibitor and angiopoietin-2 (Ang-2) inhibitor indicated for the treatment of patients with Neovascular (Wet) Age-Related Macular Degeneration (nAMD), Diabetic Macular Edema (DME), and Macular Edema following Retinal Vein Occlusion (RVO).

IMPORTANT SAFETY INFORMATION

Contraindications

VABYSMO is contraindicated in patients with ocular or periocular infection, in patients with active intraocular inflammation, and in patients with known hypersensitivity to faricimab or any of the excipients in VABYSMO.

Warnings and Precautions

- Endophthalmitis and retinal detachments may occur following intravitreal injections. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management.
- Increases in intraocular pressure have been seen within 60 minutes of an intravitreal injection.
- There is a potential risk of arterial thromboembolic events (ATEs) associated with VEGF inhibition.
- Retinal vasculitis and/or retinal vascular occlusion have been reported. Patients should be instructed to report any change in vision without delay.

Adverse Reactions

The most common adverse reactions (≥5%) reported in patients receiving VABYSMO were cataract (15%) and conjunctival hemorrhage (8%).

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555.

Please see additional Important Safety Information in the full VABYSMO Prescribing Information.

Notes

Links to Helpful Resources and Information

Genentech Ophthalmology Patient Support Services Enrollment: **Prescriber Service Form and Patient Consent Form**

My Patient Solutions® for Health Care Practices to work with Genentech Ophthalmology Access Solutions online

VABYSMO.com/support for resources for your patients and practice

The Genentech Ophthalmology Co-pay Program for more information or to enroll patients directly

Referrals to **independent co-pay assistance foundations** for patient financial support

The Access *You* Need, for the Dosing *They* Need

- Visit **VABYSMO.com/support**
- Call our Specialists at **(833) EYE-GENE**/(833) 393-4363
- Get support from a **Field Reimbursement Manager (FRM)**
- Manage your patients online with **My Patient Solutions® for Health Care Practices**

Please see Important Safety Information in the full VABYSMO Prescribing Information.

Genentech
A Member of the Roche Group

FSC CLEAR AREA
FSC FPO

FPO

VABYSMO™
faricimab-svoa injection 6 mg

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VABYSMO safely and effectively. See full prescribing information for VABYSMO.

VABYSMO® (faricimab-svoa) injection, for intravitreal use
Initial U.S. Approval: 2022

————————————RECENT MAJOR CHANGES————————————

Indications and Usage, Macular Edema Following Retinal Vein Occlusion (RVO) (1.3)	10/2023
Dosage and Administration, General Dosing Information (2.1)	7/2024
Dosage and Administration, Macular Edema Following Retinal Vein Occlusion (2.4)	10/2023
Dosage and Administration, Preparation for Administration - Prefilled Syringe (2.5)	7/2024
Dosage and Administration, Injection Procedure (2.7)	7/2024
Warnings and Precautions, Retinal Vasculitis and/or Retinal Vascular Occlusion (5.4)	10/2023

————————————INDICATIONS AND USAGE————————————

VABYSMO is a vascular endothelial growth factor (VEGF) and angiopoietin-2 (Ang-2) inhibitor indicated for the treatment of patients with:

- Neovascular (Wet) Age-Related Macular Degeneration (nAMD) (1.1)
- Diabetic Macular Edema (DME) (1.2)
- Macular Edema Following Retinal Vein Occlusion (RVO) (1.3)

————————————DOSAGE AND ADMINISTRATION————————————

For intravitreal injection. (2.1)

- Neovascular (Wet) Age-Related Macular Degeneration (nAMD)
  - The recommended dose for VABYSMO is 6 mg (0.05 mL of 120 mg/mL solution) administered by intravitreal injection every 4 weeks (approximately every 28 ± 7 days, monthly) for the first 4 doses, followed by optical coherence tomography and visual acuity evaluations 8 and 12 weeks later to inform whether to give a 6 mg dose via intravitreal injection on one of the following three 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 to every 8 weeks, some patients may need every 4 week (monthly) dosing after the first 4 doses. Patients should be assessed regularly. (2.2)
- Diabetic Macular Edema (DME)
  - VABYSMO is recommended to be dosed by following one of these two dose regimens: 1) 6 mg (0.05 mL of 120 mg/mL solution) administered by intravitreal injection every 4 weeks (approximately every 28 days ± 7 days, monthly) for at least 4 doses. If after at least 4 doses, resolution of edema based on the central subfield thickness (CST) of the macula as measured by optical coherence tomography is achieved, then the interval of dosing 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; or 2) 6 mg dose of VABYSMO can be administered every 4 weeks for the first 6 doses, followed by 6 mg dose via intravitreal injection at intervals of every 8 weeks (2 months). Although additional efficacy was not demonstrated in most patients when VABYSMO was dosed every 4 weeks compared to every 8 weeks, some patients may need every 4 week (monthly) dosing after the first 4 doses. Patients should be assessed regularly. (2.3)
- Macular Edema Following Retinal Vein Occlusion (RVO)
  - The recommended dose for VABYSMO is 6 mg (0.05 mL of 120 mg/mL) administered by intravitreal injection every 4 weeks (approximately every 28 ± 7 days, monthly) for 6 months. (2.4)

————————————DOSAGE FORMS AND STRENGTHS————————————

- Injection: 6 mg (0.05 mL of 120 mg/mL solution) in a single-dose prefilled syringe (3)
- Injection: 6 mg (0.05 mL of 120 mg/mL solution) in a single-dose vial (3)

————————————CONTRAINDICATIONS————————————

- Ocular or periocular infection (4.1)
- Active intraocular inflammation (4.2)
- Hypersensitivity (4.3)

————————————WARNINGS AND PRECAUTIONS————————————

- Endophthalmitis and retinal detachments may occur following intravitreal injections. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management. (5.1)
- Increases in intraocular pressure have been seen within 60 minutes of an intravitreal injection. (5.2)
- There is a potential risk of arterial thromboembolic events (ATEs) associated with VEGF inhibition. (5.3)

————————————ADVERSE REACTIONS————————————

The most common adverse reactions (≥ 5%) reported in patients receiving VABYSMO were cataract (15%) and conjunctival hemorrhage (8%). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 7/2024

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

VABYSMO is a vascular endothelial growth factor (VEGF) and angiopoietin 2 (Ang-2) inhibitor indicated for the treatment of patients with:

1.1 Neovascular (wet) Age-Related Macular Degeneration (nAMD)
1.2 Diabetic Macular Edema (DME)
1.3 Macular Edema Following Retinal Vein Occlusion (RVO)

2 DOSAGE AND ADMINISTRATION

2.1 General Dosing Information

For intravitreal injection. VABYSMO must be administered by a qualified physician.

VABYSMO is available as:

- Prefilled syringe: A sterile injection filter needle (30-gauge x ½-inch, Extra Thin Wall) with an integrated filter in the hub is provided. Each prefilled syringe should only be used for the treatment of a single eye.
- Vial: A sterile 5-micron, blunt transfer filter needle (18-gauge x 1½-inch) is provided. Each vial should only be used for the treatment of a single eye.

[see How Supplied/Storage and Handling (16)]

2.2 Neovascular (wet) Age-Related Macular Degeneration (nAMD)

The recommended dose for VABYSMO is 6 mg (0.05 mL of 120 mg/mL solution) administered by intravitreal injection every 4 weeks (approximately every 28 ± 7 days, monthly) for the first 4 doses, followed by optical coherence tomography and visual acuity evaluations 8 and 12 weeks later to inform whether to give a 6 mg dose via intravitreal injection on one of the following three 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 to every 8 weeks, some patients may need every 4 week (monthly) dosing after the first 4 doses. Patients should be assessed regularly.

2.3 Diabetic Macular Edema (DME)

VABYSMO is recommended to be dosed by following one of these two dose regimens: 1) 6 mg (0.05 mL of 120 mg/mL solution) administered by intravitreal injection every 4 weeks (approximately every 28 days ± 7 days, monthly) for at least 4 doses. If after at least 4 doses, resolution of edema based on the central subfield thickness (CST) of the macula as measured by optical coherence tomography is achieved, then the interval of dosing 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; or 2) 6 mg dose of VABYSMO can be administered every 4 weeks for the first 6 doses, followed by 6 mg dose via intravitreal injection at intervals of every 8 weeks (2 months). Although additional efficacy was not demonstrated in most patients when VABYSMO was dosed every 4 weeks compared to every 8 weeks, some patients may need every 4 week (monthly) dosing after the first 4 doses. Patients should be assessed regularly.

2.4 Macular Edema Following Retinal Vein Occlusion (RVO)

The recommended dose for VABYSMO is 6 mg (0.05 mL of 120 mg/mL solution) administered by intravitreal injection every 4 weeks (approximately every 28 ± 7 days, monthly) for 6 months.

2.5 Preparation for Administration - Prefilled Syringe

Before you start

Read all the instructions carefully before using VABYSMO.

The VABYSMO carton includes:

A sterile prefilled syringe in a sealed tray. The prefilled syringe is for treatment of a single eye.

A sterile injection filter needle (30-gauge x ½ inch, Extra Thin Wall) with an integrated filter in the hub. The injection filter needle is for single use only.

Only use the provided injection filter needle for the administration.

VABYSMO should be refrigerated at temperatures between 2ºC to 8ºC (36ºF to 46ºF).
Do not freeze.

Allow VABYSMO to reach room temperature, 20°C to 25°C (68°F to 77°F) before proceeding with the administration.

Prior to use, keep the sealed tray in the original carton to **protect the prefilled syringe from light**. The prefilled syringe may be kept at room temperature in the original carton for up to **24 hours**.

VABYSMO should be inspected visually prior to administration.

Do not use if the carton seals have been tampered with.

Do not use if the packaging, prefilled syringe, injection filter needle is expired, damaged, or have been tampered with.

Do not use if the injection filter needle is missing.

Do not remove the finger grip from the syringe.

Do not use if the syringe cap is detached from the Luer lock.

Do not use if particulates, cloudiness, or discoloration are visible. VABYSMO is a clear to opalescent and colorless to brownish-yellow liquid solution.

Prefilled Syringe Description

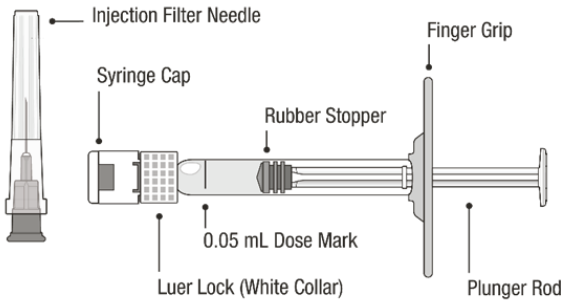


Figure A

Note: the dose must be set to the 0.05 mL dose mark.

Use aseptic technique to carry out the following preparation steps:

Open Tray and Remove Syringe Cap

1 Peel the lid off the syringe tray and aseptically remove the prefilled syringe.

2 Hold the syringe by the white collar; snap off the syringe cap (**see Figure B**).

Do not twist off the cap.

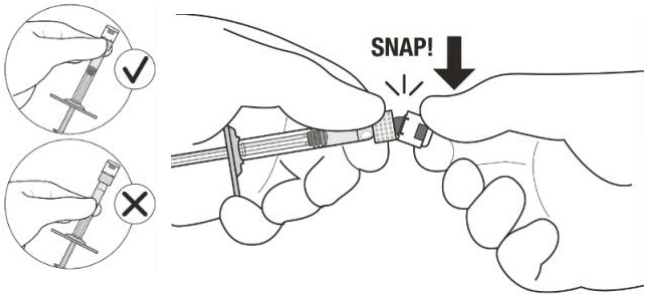


Figure B

Attach Injection Filter Needle

3 Aseptically remove the provided injection filter needle from its packaging.

4 Aseptically and firmly attach the injection filter needle onto the syringe Luer lock (**see Figure C**).

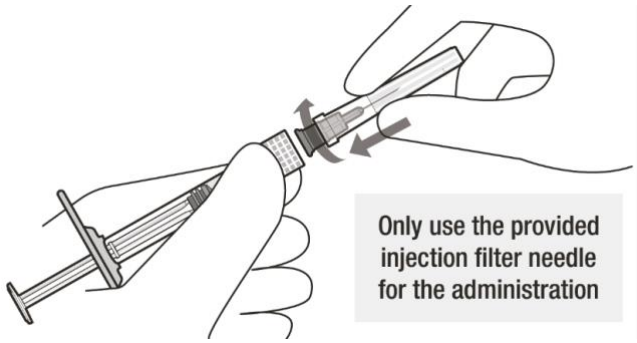


Figure C

5 Carefully remove the needle cap by pulling it straight off.

Dislodge Air Bubbles

6 Hold the syringe with the injection filter needle pointing up. Check the syringe for air bubbles.

---

7 If there are any air bubbles, gently tap the syringe with your finger until the bubbles rise to the top (**see Figure D**).

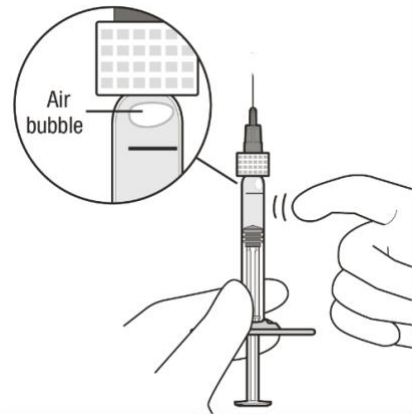


Figure D

Expel Air and Adjust the Dose

8 Hold the syringe at eye level and **slowly** push the plunger rod until the **lower edge of the rubber stopper's dome** is aligned with the 0.05 mL dose mark (**see Figure E**). This will expel the air and the excess solution and set the dose to 0.05 mL.

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

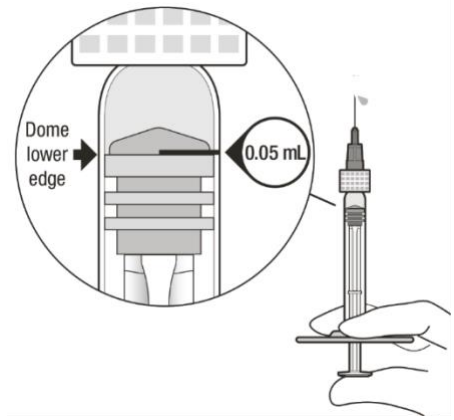


Figure E

2.6 Preparation for Administration - Vial

Before you start

Read all the instructions carefully before using VABYSMO.

The VABYSMO kit includes a glass vial and transfer filter needle. The glass vial is for a single dose only. The filter needle is for treatment of a single eye.

VABYSMO should be stored refrigerated at temperatures between 2ºC to 8ºC (36ºF to 46ºF).
Do not freeze.
Do not shake.

Allow VABYSMO to reach room temperature, 20°C to 25°C (68°F to 77°F) before proceeding with the administration. Keep the vial in the original carton to **protect from light.**
The VABYSMO vial may be kept at room temperature for up to **24 hours**.

The VABYSMO vial should be inspected visually for particulate matter and discoloration prior to administration. VABYSMO is a clear to opalescent and colorless to brownish-yellow liquid solution.
Do not use if particulates, cloudiness, or discoloration are visible.
Do not use if the packaging, vial and/or transfer filter needle are expired, damaged, or have been tampered with (see **Figure F**).

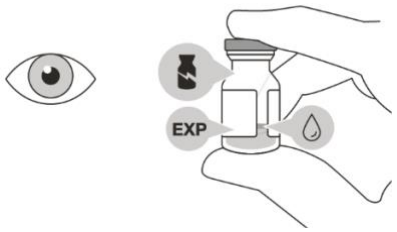


Figure F

Use aseptic technique to carry out the preparation of the intravitreal injection.

1 Gather the following supplies:

- One VABYSMO vial (included)
- One sterile 5-micron blunt transfer filter needle 18-gauge x 1½ inch (included)
- One sterile 1 mL Luer lock syringe with a 0.05 mL dose mark (**not included**)
- One sterile injection needle 30-gauge x ½ inch (**not included**)
  Note that a 30-gauge injection needle is recommended to avoid increased injection forces that could be experienced with smaller diameter needles.
- Alcohol swab (**not included**).

2 To ensure all liquid settles at the bottom of the vial, place the vial upright on a flat surface (for about 1 minute) after removal from packaging (see **Figure G**). Gently tap the vial with your finger (see **Figure H**), as liquid may stick to the top of the vial.

Figure G

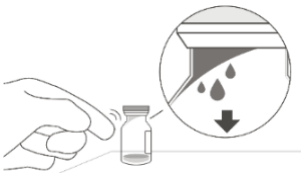


Figure H

3 Remove the flip-off cap from the vial (see **Figure I**) and wipe the vial septum with an alcohol swab (see **Figure J**).

Figure I

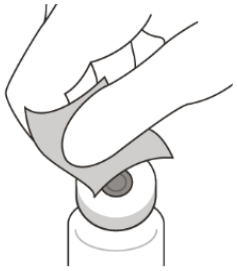


Figure J

4 Aseptically and firmly attach the included 18-gauge x 1½ inch transfer filter needle onto a 1 mL Luer lock syringe (see **Figure K**).

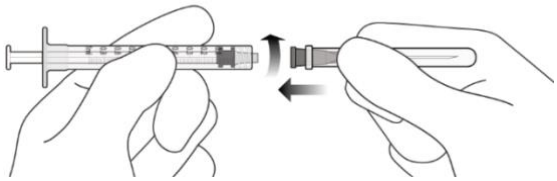


Figure K

5 Using aseptic technique, push the transfer filter needle into the center of the vial septum (see **Figure L**), push it all the way in, then tilt the vial slightly so that the needle touches the bottom edge of the vial (see **Figure M**).

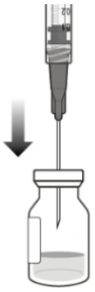


Figure L

Figure M

6 Hold the vial slightly inclined and **slowly** withdraw all the liquid from the vial (see **Figure N**). Keep the bevel of the transfer filter needle submerged in the liquid, to avoid introduction of air.

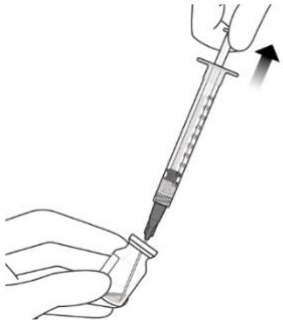


Figure N

7	Ensure that the plunger rod is drawn sufficiently back when emptying the vial, in order to completely empty the transfer filter needle (see **Figure N**).
8	Disconnect the transfer filter needle from the syringe and dispose of it in accordance with local regulations. **Do not use the transfer filter needle for the intravitreal injection.**
9	Aseptically and firmly attach a 30-gauge x ½ inch injection needle onto the Luer lock syringe (see **Figure O**).

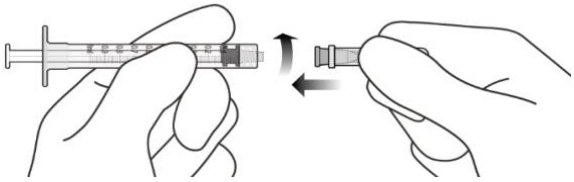


Figure O

10	Carefully remove the plastic needle shield from the needle by pulling it straight off.
11	To check for air bubbles, hold the syringe with the needle pointing up. If there are any air bubbles, gently tap the syringe with your finger until the bubbles rise to the top (see **Figure P**).

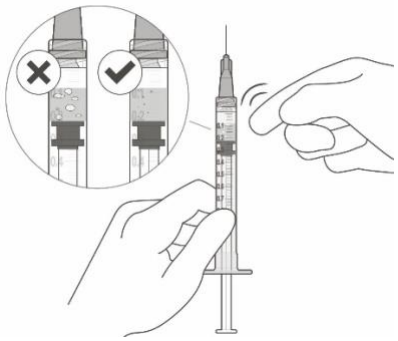


Figure P

12	Carefully expel the air from the syringe and needle, and **slowly** depress the plunger to align the rubber stopper tip to the 0.05 mL dose mark. The syringe is ready for the injection (see **Figure Q**). Ensure that the injection is given **immediately** after preparation of the dose.

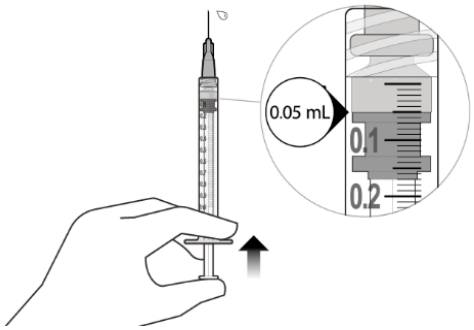


Figure Q

2.7 Injection Procedure

The intravitreal injection procedure must be carried out under aseptic conditions, which includes the use of surgical hand disinfection, sterile gloves, a sterile drape and a sterile eyelid speculum (or equivalent), and the availability of sterile paracentesis equipment (if required). Adequate anesthesia and a broad-spectrum microbicide should be administered prior to the injection.

Inject **slowly** until the rubber stopper reaches the end of the syringe to deliver the volume of 0.05 mL.

Note for the prefilled syringe: **Do not** recap or detach the injection filter needle from the syringe.

Any unused drug product or waste material should be disposed of in accordance with local regulations.

Immediately following the intravitreal injection, patients should be monitored for elevation in intraocular pressure. Appropriate monitoring may consist of a check for perfusion of the optic nerve head or tonometry. If required, a sterile paracentesis needle should be available. Following intravitreal injection, patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment (e.g., vision loss, eye pain, redness of the eye, photophobia, blurring of vision) without delay *[see Patient Counseling Information (17)]*.

Each syringe should only be used for the treatment of a single eye. If the contralateral eye requires treatment, a new syringe should be used and the sterile field, syringe, gloves, drapes, eyelid speculum, filter, and injection needles should be changed before VABYSMO is administered to the other eye.

3 DOSAGE FORMS AND STRENGTHS

VABYSMO is a clear to opalescent, colorless to brownish-yellow solution available as:

- Injection: 6 mg (0.05 mL of 120 mg/mL solution) in a single-dose prefilled glass syringe
- Injection: 6 mg (0.05 mL of 120 mg/mL solution) in a single-dose glass vial

4 CONTRAINDICATIONS

4.1 Ocular or Periocular Infections

VABYSMO is contraindicated in patients with ocular or periocular infections.

4.2 Active Intraocular Inflammation
VABYSMO is contraindicated in patients with active intraocular inflammation.

4.3 Hypersensitivity
VABYSMO is contraindicated in patients with known hypersensitivity to faricimab or any of the excipients in VABYSMO. Hypersensitivity reactions may manifest as rash, pruritus, urticaria, erythema, or severe intraocular inflammation.

5 WARNINGS AND PRECAUTIONS
5.1 Endophthalmitis and Retinal Detachments
Intravitreal injections, including Vabysmo, have been associated with endophthalmitis and retinal detachments *[see Adverse Reactions (6.1)]*. Proper aseptic injection techniques must always be used when administering VABYSMO. Patients should be instructed to report any signs or symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management *[see Dosage and Administration (2.6) and Patient Counseling Information (17)]*.

5.2 Increase in Intraocular Pressure
Transient increases in intraocular pressure (IOP) have been seen within 60 minutes of intravitreal injection, including with VABYSMO *[see Adverse Reactions (6.1)]*. IOP and the perfusion of the optic nerve head should be monitored and managed appropriately *[see Dosage and Administration (2.6)]*.

5.3 Thromboembolic Events
Although there was a low rate of arterial thromboembolic events (ATEs) observed in the VABYSMO clinical trials, there is a potential risk of ATEs following intravitreal use of VEGF inhibitors. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause).

The incidence of reported ATEs in the nAMD studies during the first year was 1% (7 out of 664) in patients treated with VABYSMO compared with 1% (6 out of 662) in patients treated with aflibercept *[see Clinical Studies (14.1)]*.

The incidence of reported ATEs in the DME studies from baseline to week 100 was 5% (64 out of 1,262) in patients treated with VABYSMO compared with 5% (32 out of 625) in patients treated with aflibercept *[see Clinical Studies (14.2)]*.

The incidence of reported ATEs in the RVO studies during the first 6 months was 1.1% (7 out of 641) in patients treated with VABYSMO compared with 1.4% (9 out of 635) in patients treated with aflibercept *[see Clinical Studies (14.3)]*.

5.4 Retinal Vasculitis and/or Retinal Vascular Occlusion
Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, have been reported with the use of VABYSMO *[see Adverse Reactions (6.2)]*. Discontinue treatment with VABYSMO in patients who develop these events. Patients should be instructed to report any change in vision without delay.

6 ADVERSE REACTIONS
The following potentially serious adverse reactions are described elsewhere in the labeling:
- Hypersensitivity *[see Contraindications (4)]*
- Endophthalmitis and retinal detachments *[see Warnings and Precautions (5.1)]*

- Increase in intraocular pressure *[see Warnings and Precautions (5.2)]*
- Thromboembolic events *[see Warnings and Precautions (5.3)]*
- Retinal Vasculitis and/or Retinal Vascular Occlusion *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in other clinical trials of the same or another drug and may not reflect the rates observed in practice.

The data described below reflect exposure to VABYSMO in 2,567 patients, which constituted the safety population in six Phase 3 studies *[see Clinical Studies (14.1, 14.2, 14.3)]*.

Table 1: Common Adverse Reactions (≥ 1%)

Adverse Reactions	**VABYSMO**			**Active Control (aflibercept)**		
	AMD N=664	**DME N=1,262**	**RVO N=641**	**AMD N=662**	**DME N=625**	**RVO N=635**
Cataract	3%	15%	< 1%	2%	12%	1%
Conjunctival hemorrhage	7%	8%	3%	8%	7%	4%
Vitreous detachment	3%	5%	2%	3%	4%	2%
Vitreous floaters	3%	4%	2%	2%	3%	2%
Retinal pigment epithelial tear[a]	3%			1%		
Intraocular pressure increased	3%	4%	1%	2%	3%	3%
Eye pain	3%	3%	< 1%	3%	3%	< 1%
Intraocular inflammation[b]	2%	1%	1%	1%	1%	< 1%
Eye irritation	1%	< 1%	< 1%	< 1%	1%	< 1%
Lacrimation increased	1%	1%	0	1%	< 1%	< 1%
Ocular discomfort	1%	1%	< 1%	< 1%	< 1%	< 1%

[a] AMD only
[b] Including iridocyclitis, iritis, uveitis, vitritis

Less common adverse reactions reported in < 1% of the patients treated with VABYSMO were corneal abrasion, eye pruritus, ocular hyperemia, blurred vision, sensation of foreign body, endophthalmitis, conjunctival hyperaemia, visual acuity reduced, visual acuity reduced transiently, vitreous hemorrhage, retinal tear and rhegmatogenous retinal detachment.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of VABYSMO. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Eye disorders: retinal vasculitis with or without retinal vascular occlusion.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies of VABYSMO administration in pregnant women.

Administration of VABYSMO to pregnant monkeys throughout the period of organogenesis resulted in an increased incidence of abortions at intravenous (IV) doses 158 times the human exposure (based on C_{max}) of the maximum recommended human dose *[see Animal Data]*. Based on the mechanism of action of VEGF and Ang-2 inhibitors, there is a potential risk to female

reproductive capacity, and to embryo-fetal development. VABYSMO should not be used during pregnancy unless the potential benefit to the patient outweighs the potential risk to the fetus.

All pregnancies have a background risk of birth defect, loss, and other adverse outcomes. The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects is 2%-4% and of miscarriage is 15%-20% of clinically recognized pregnancies.

Data

Animal Data

An embryo fetal developmental toxicity study was performed on pregnant cynomolgus monkeys. Pregnant animals received 5 weekly IV injections of VABYSMO starting on day 20 of gestation at 1 or 3 mg/kg. A non-dose dependent increase in pregnancy loss (abortions) was observed at both doses evaluated. Serum exposure (C_{max}) in pregnant monkeys at the low dose of 1 mg/kg was 158 times the human exposure at the maximum recommended intravitreal dose of 6 mg once every 4 weeks. A no observed adverse effect level (NOAEL) was not identified in this study.

8.2 Lactation

Risk Summary

There is no information regarding the presence of faricimab in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production. Many drugs are transferred in human milk with the potential for absorption and adverse reactions in the breastfed child.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for VABYSMO and any potential adverse effects on the breastfed child from VABYSMO.

8.3 Females and Males of Reproductive Potential

Contraception

Females of reproductive potential are advised to use effective contraception prior to the initial dose, during treatment and for at least 3 months following the last dose of VABYSMO.

Infertility

No studies on the effects of faricimab on human fertility have been conducted and it is not known whether faricimab can affect reproduction capacity. Based on the mechanism of action, treatment with VABYSMO may pose a risk to reproductive capacity.

8.4 Pediatric Use

The safety and efficacy of VABYSMO in pediatric patients have not been established.

8.5 Geriatric Use

In the six clinical studies, approximately 58% (1,496/2,571) of patients randomized to treatment with VABYSMO were ≥ 65 years of age. No significant differences in efficacy or safety of faricimab were seen with increasing age in these studies. No dose adjustment is required in patients 65 years and above.

11 DESCRIPTION

Faricimab-svoa is a humanized bispecific immunoglobulin G1 (IgG1) antibody that binds both vascular endothelial growth factor A (VEGF-A) and angiopoietin-2 (Ang-2). The fragment crystallizable (Fc) region of faricimab was engineered by selected point mutations to abolish binding interactions with Fcγ and FcRn receptors. Faricimab-svoa has a total molecular weight of approximately 149 kDa and is produced by recombinant DNA technology using mammalian Chinese Hamster Ovary (CHO) cell culture.

VABYSMO (faricimab-svoa) injection is a sterile, clear to opalescent, colorless to brownish-yellow solution in a single-dose prefilled glass syringe or glass vial for intravitreal administration. Each single-dose prefilled syringe or single-dose vial is designed to deliver 0.05 mL (50 microliters) of solution containing 6 mg faricimab-svoa, L-histidine (155 mcg), L-methionine (52.2 mcg), polysorbate 20 (20 mcg), sodium chloride (73.1 mcg), D-sucrose (2.74 mg) and Water for Injection, adjusted to pH 5.5 with acetic acid. The product does not contain an anti-microbial preservative.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Faricimab is a humanized bispecific antibody that acts through inhibition of two 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. Ang-2 levels are increased in some patients with nAMD, DME, and RVO. The contribution of Ang-2 inhibition to the treatment effect and clinical response for nAMD, DME, and RVO has yet to be established.

12.2 Pharmacodynamics

Increased retinal thickness, assessed by optical coherence tomography (OCT), is associated with nAMD, DME and macular edema following RVO. Leakage of blood and fluid from choroidal neovascularization, assessed by fluorescein angiography, is associated with nAMD. Reductions in CST were observed across all treatment arms throughout the six Phase 3 studies in nAMD, DME, and RVO.

12.3 Pharmacokinetics

Absorption/Distribution

Maximum faricimab plasma concentrations (Cmax) are estimated to occur approximately 2 days post-dose. Mean (±SD) free faricimab (unbound to VEGF-A and Ang-2) plasma Cmax are estimated to be 0.23 (0.07) mcg/mL and 0.22 (0.07) mcg/mL in nAMD and in DME patients, respectively. After repeated intravitreal administrations, mean plasma free faricimab trough concentrations are predicted to be 0.002-0.003 mcg/mL for every 8 weeks (Q8W) dosing and 0.021-0.029 mcg/mL for every 4 weeks (Q4W) dosing. Although not directly measured in the vitreous, no accumulation of faricimab is expected in the vitreous and no accumulation has been observed in plasma when faricimab has been administered as repeat doses in the vitreous.

Metabolism/Elimination

Metabolism and elimination of faricimab has not been fully characterized. Faricimab is expected to be catabolized in lysosomes to small peptides and amino acids, which may be excreted renally, in a similar manner to the elimination of endogenous IgG. The estimated mean apparent systemic half-life of faricimab is approximately 7.5 days.

Specific Populations
The systemic pharmacokinetics of faricimab were not influenced by gender, race, or mild to severe renal impairment (i.e., estimated normalized creatinine clearance by Cockroft-Gault equation: 15 to 89 mL/min/1.73 m^2). The effect of severe renal impairment or any degree of hepatic impairment on the pharmacokinetics of VABYSMO is unknown. No special dosage modification is required for any of the populations that have been studied (e.g., elderly, gender, race).

Population pharmacokinetic analysis indicated that the pharmacokinetics of faricimab are comparable in nAMD, DME, and RVO patients.

12.6 Immunogenicity
The immunogenicity of VABYSMO was evaluated in plasma samples. The immunogenicity data reflect the percentage of patients whose test results were considered positive for antibodies to VABYSMO in immunoassays. The detection of an immune response is highly dependent on the sensitivity and specificity of the assays used, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to VABYSMO with the incidence of antibodies to other products may be misleading.

There is a potential for an immune response in patients treated with VABYSMO. In the nAMD, DME, and RVO studies, the pre-treatment incidence of anti-faricimab antibodies was approximately 0.8 to 1.8%. After initiation of dosing, the incidence of anti-faricimab antibodies was approximately 8% to 10.4% in patients treated with VABYSMO across studies. As with all therapeutic proteins, there is a potential for immunogenicity with VABYSMO.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
No carcinogenicity or mutagenicity data are available for VABYSMO injection in animals or humans.

Based on the anti-VEGF and Ang-2 mechanisms of action, treatment with VABYSMO may pose a risk to reproductive capacity *[see Females and Males of Reproductive Potential (8.3)]*.

14 CLINICAL STUDIES
14.1 Neovascular (wet) Age-Related Macular Degeneration (nAMD)
The safety and efficacy of VABYSMO were assessed in two randomized, multi-center, double-masked, active comparator-controlled, 2-year studies (TENAYA – NCT03823287 and LUCERNE – NCT03823300) in patients with nAMD.

A total of 1,329 newly diagnosed, treatment-naïve patients were enrolled in these studies, and 664 patients received at least one dose of VABYSMO. Patient ages ranged from 50 to 99 with a mean of 75.9 years. The studies were identically designed two year studies. Patients were randomized in a 1:1 ratio to one of two treatment arms: 1) aflibercept 2 mg administered fixed every 8 weeks (Q8W) after three initial monthly doses; and VABYSMO 6 mg (0.05 mL of 120 mg/mL solution) administered by intravitreal injection every 4 weeks (approximately every 28 ± 7 days, monthly) 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 6 mg (0.05 mL of 120 mg/mL solution) dose via intravitreal injection on one of the following three 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). However, the utility of these criteria to guide dosing intervals has not been established.

At week 48, after 4 initial monthly doses in the VABYSMO arm, 45% of patients received the Weeks 28 and 44 dosing, 33% of patients received the Weeks 24, 36 and 48 dosing, and the remaining 22% of patients received dosing every 8 weeks. These percentages are reflective of what happened within the conduct of these trials and indicate that some patients did well on two (2) doses spaced 16 weeks apart, or three (3) doses spaced 12 weeks apart, but the percentages may not be generalizable to a broader nAMD population for a variety of reasons. The inclusion/exclusion criteria limited enrollment to a select subset of treatment-naïve, newly diagnosed nAMD patients and there is no empirical data that a similar magnitude would be observed if eligibility criteria allowed for broader enrollment. The disease activity criteria, which was instrumental in determining dose frequency, is unvalidated. Stricter criteria would have changed how patients were treated resulting in different percentages of subjects in each dose interval cohort. There was not a similarly dosed aflibercept arm for comparison, which makes the percentages difficult to interpret.

Both studies demonstrated non-inferiority to the comparator control (aflibercept) at the primary endpoint, defined as the mean 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. The primary endpoint analysis was a non-inferiority comparison for the mean change in BCVA between the aflibercept and the VABYSMO arm. The lower bound of the 95% confidence interval for the mean change in BCVA could not be lower than minus 4 letters to declare non-inferiority. In both studies, VABYSMO treated patients had a non-inferior mean change from baseline in BCVA compared to patients treated with aflibercept. Detailed results of both studies are shown in Table 2, Figure 1, and Figure 2 below. The clinical efficacy for the second year of the study has not been reviewed.

Table 2: Primary Endpoint Results[a] in the TENAYA and LUCERNE Studies

	TENAYA		**LUCERNE**	
	VABYSMO N = 334	**Aflibercept N = 337**	**VABYSMO N = 331**	**Aflibercept N = 327**
Mean change in BCVA as measured by ETDRS letter score from baseline (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)	

[a] Average of weeks 40, 44 and 48
BCVA: Best Corrected Visual Acuity
ETDRS: Early Treatment Diabetic Retinopathy Study
CI: Confidence Interval
LS: Least Square

Figure 1: Mean Change in Visual Acuity from Baseline to Week 48 in TENAYA

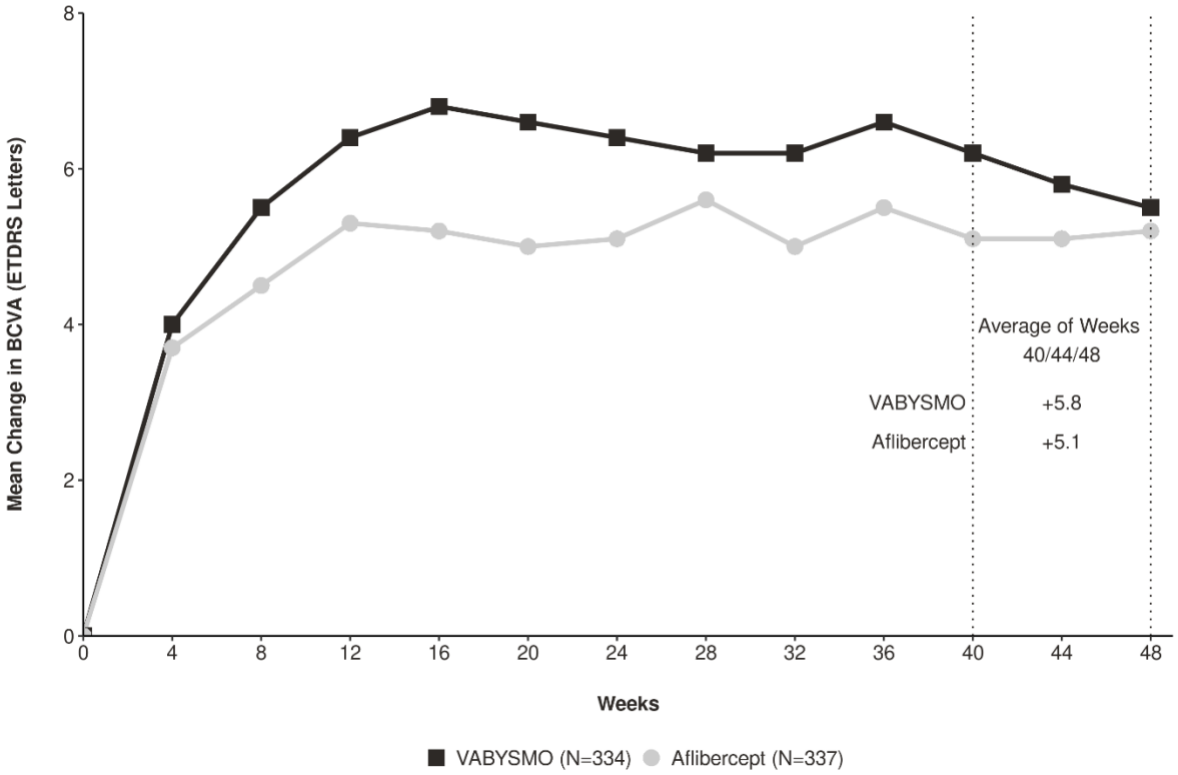
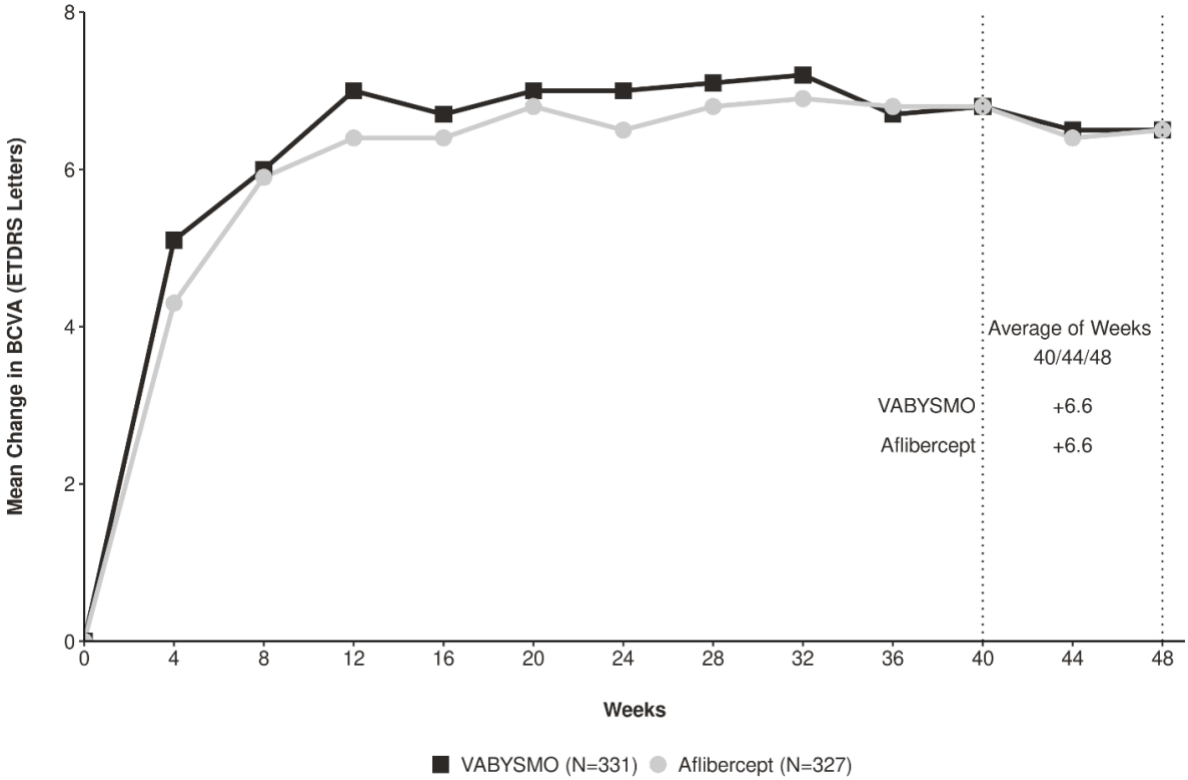


Figure 2: Mean Change in Visual Acuity from Baseline to Week 48 in LUCERNE



Treatment effects in evaluable subgroups (e.g., age, gender, race, baseline visual acuity) in each study were consistent with the results in the overall population.

14.2 Diabetic Macular Edema (DME)

The safety and efficacy of VABYSMO were assessed in two randomized, multi-center, double-masked, active comparator-controlled 2-year studies (YOSEMITE – NCT03622580 and RHINE – NCT03622593) in patients with DME.

A total of 1,891 diabetic patients were enrolled in the two studies with a total of 1,262 patients treated with at least one dose of VABYSMO. Patient ages ranged from 24 to 91 with a mean of 62.2 years. The overall population included both anti-VEGF naïve patients (78%) and patients who had been previously treated with a VEGF inhibitor prior to study participation (22%).

The studies were identically designed two year studies. Patients were randomized in a 1:1:1 ratio to one of three treatment regimens: 1) aflibercept Q8W, patients received fixed aflibercept 2 mg administered every 8 weeks (Q8W) after the first five monthly doses; 2) VABYSMO Q8W, patients received fixed VABYSMO 6 mg administered Q8W after the first six monthly doses; and 3) VABYSMO Variable, patients received VABYSMO 6 mg administered every 4 weeks for at least 4 doses and until the central subfield thickness (CST) of the macula measured by optical coherence tomography was less than approximately 325 microns, then the interval of dosing was modified by up to 4 week interval extensions or reductions of up to 8 week interval increments based on CST and visual acuity disease activity criteria at study drug dosing visits.

After 4 initial monthly doses, the patients in the VABYSMO Variable arm received between a minimum of 1 and a maximum of 21 total injections (median of 7 injections) through Week 96 inclusive. At Week 56, 32% of patients had completed at least one Q12W interval followed by one full Q16W interval. Seventeen percent (17%) of patients were treated on Q8W and/or Q4W dosing intervals through Week 56 (7% only on Q4W). These percentages are reflective of what happened within the conduct of these trials, but the percentages may not be generalizable to a broader DME population.

The inclusion/exclusion criteria limited enrollment to a select subset of DME patients and there is no empirical data that a similar magnitude would be observed if eligibility criteria allowed for broader enrollment. The disease activity criteria, which were instrumental in determining dose frequency, are unvalidated. Different criteria would have changed how patients were treated resulting in different percentages of subjects in each dose interval cohort. There was not a similarly dosed aflibercept arm for comparison which makes the percentages difficult to interpret.

Both studies demonstrated non-inferiority to the comparator control (aflibercept) at the primary endpoint, defined as the mean change from baseline in BCVA at year 1 (average of the Week 48, 52, and 56 visits), measured by the ETDRS Letter Score. The primary endpoint analysis was a non-inferiority comparison for the mean change in BCVA between the aflibercept and VABYSMO arms. The lower bound of the 97.5% confidence interval for the mean change in BCVA could not be lower than minus 4 letters to declare non-inferiority. In both studies, VABYSMO Q8W and VABYSMO Variable treated patients had a non-inferior mean change from baseline in BCVA to the patients treated with aflibercept Q8W at the year 1 primary endpoint. Detailed results of both studies are shown in Table 3, Figure 3, and Figure 4 below.

Table 3: Efficacy Results at Year 1[a] and at Year 2[b] in the YOSEMITE and RHINE Studies

	YOSEMITE						RHINE					
	Year 1			Year 2			Year 1			Year 2		
	VABYSMO Q8W N = 315	VABYSMO Variable N = 313	Aflibercept Q8W N = 312	VABYSMO Q8W N = 262	VABYSMO Variable N = 270	Aflibercept Q8W N = 259	VABYSMO Q8W N = 317	VABYSMO Variable N = 319	Aflibercept Q8W N = 315	VABYSMO Q8W N = 259	VABYSMO Variable N = 282	Aflibercept Q8W N = 254
Mean change in BCVA as measured by ETDRS letter score from baseline (97.5% CI year 1 and 95% CI year 2)	10.7 (9.4, 12.0)	11.6 (10.3, 12.9)	10.9 (9.6, 12.2)	10.7 (9.4, 12.1)	10.7 (9.4, 12.1)	11.4 (10.0, 12.7)	11.8 (10.6, 13.0)	10.8 (9.6, 11.9)	10.3 (9.1, 11.4)	10.9 (9.5, 12.3)	10.1 (8.7, 11.5)	9.4 (7.9, 10.8)
Difference in LS mean (97.5% CI year 1 and 95% CI year 2)	-0.2 (-2.0, 1.6)	0.7 (-1.1, 2.5)		-0.7[c]	-0.7[c]		1.5 (-0.1, 3.2)	0.5 (-1.1, 2.1)		1.5[c]	0.7[c]	

[a]Average of Weeks 48, 52, 56
[b]Average of Weeks 92, 96, 100
[c]A non-inferiority margin was not available for year 2
BCVA: Best Corrected Visual Acuity
ETDRS: Early Treatment Diabetic Retinopathy Study
CI: Confidence Interval
LS: Least Square

Figure 3: Mean Change in Visual Acuity from Baseline to Year 2 (Week 100) in YOSEMITE

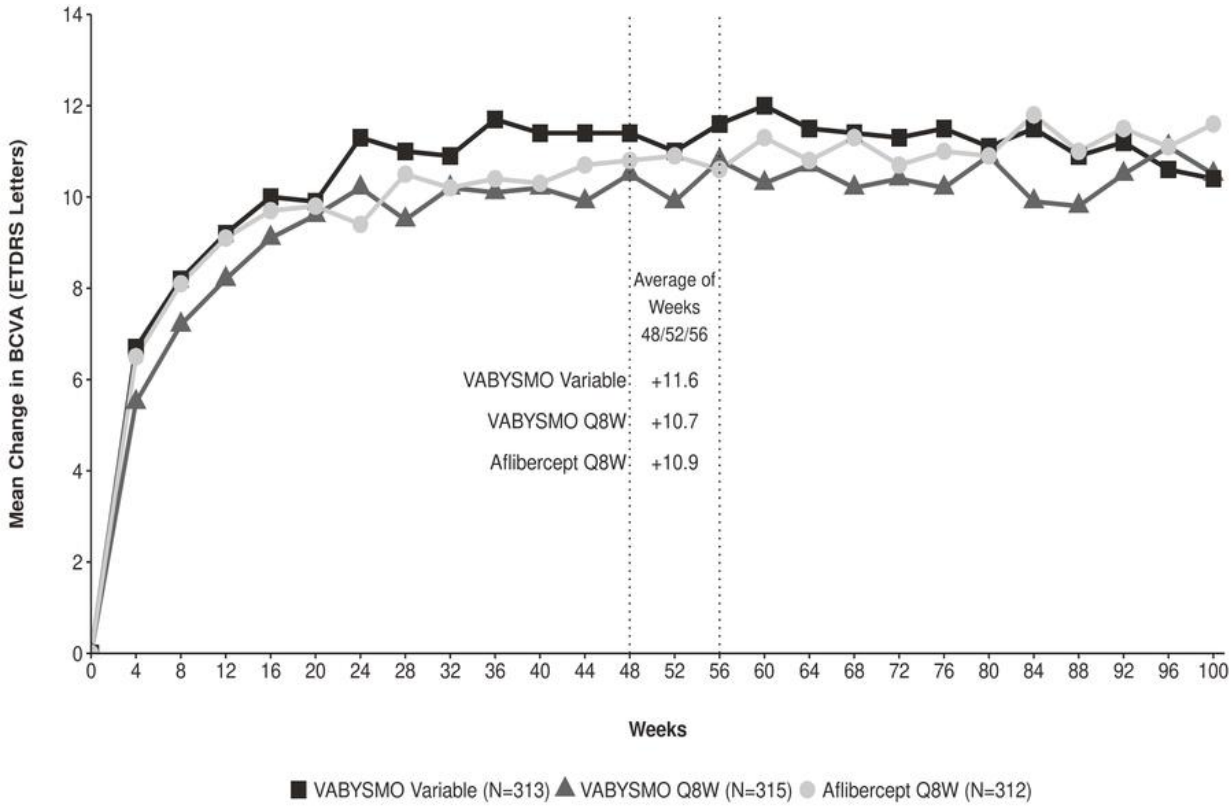
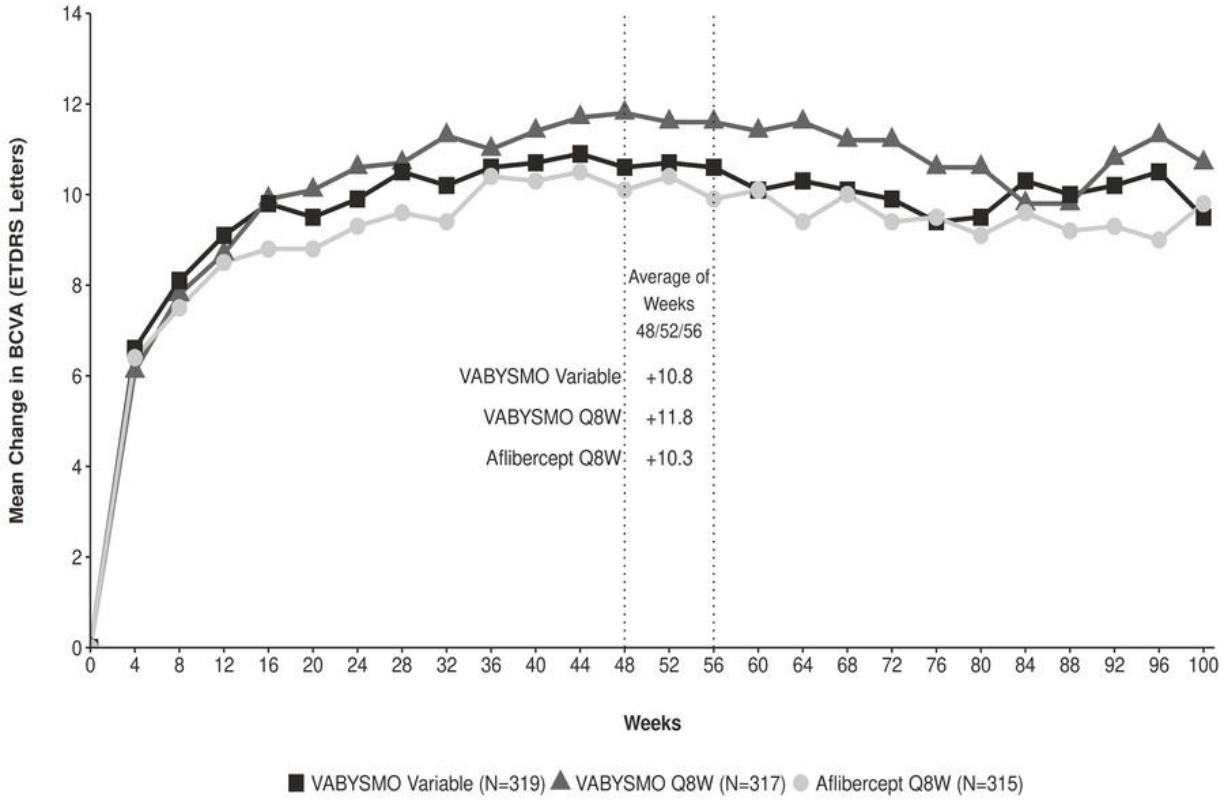


Figure 4: Mean Change in Visual Acuity from Baseline to Year 2 (Week 100) in RHINE



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. Treatment effects in evaluable subgroups (e.g., by age, gender, race, baseline HbA1c, baseline visual acuity) in each study were generally consistent with the results in the overall population.

14.3 Macular Edema Following Retinal Vein Occlusion (RVO)

The safety and efficacy of VABYSMO were assessed in two randomized, multicenter, double-masked, studies (BALATON – NCT04740905 in patients with macular edema following branch retinal vein occlusion, and COMINO – NCT04740931 in patients with macular edema following central retinal vein occlusion/hemiretinal vein occlusion). Active comparator-controlled data are available through month 6.

A total of 1,282 newly diagnosed, treatment-naïve patients were enrolled in these studies, of which 641 patients received at least one dose of VABYSMO through 6 months. Patient ages ranged from 28 to 93 with a mean of 64 years, and 22 to 100 with a mean of 65 years in BALATON and COMINO, respectively.

In both studies, patients were randomized in a 1:1 ratio to either 6 mg VABYSMO administered every 4 weeks, or the control arm receiving aflibercept 2 mg injections every 4 weeks for a total of 6 injections.

In both studies, the VABYSMO 6 mg Q4W arm demonstrated non-inferiority to the comparator control (aflibercept) arm for the primary endpoint, which was defined as the change from baseline in BCVA at week 24, measured by the ETDRS Letter Score. The primary endpoint analysis was a non-inferiority comparison for the mean change in BCVA between the aflibercept and VABYSMO arms, where the lower bound of the 95% confidence interval for the mean change in BCVA could not be lower than minus 4 letters to declare non-inferiority.

Detailed results for both BALATON and COMINO studies are shown in Table 4, Figure 5, and Figure 6 below.

Table 4: Primary Endpoint Results at Week 24 in the BALATON and COMINO Studies

	BALATON		**COMINO**	
	VABYSMO N = 276	**Aflibercept N = 277**	**VABYSMO N = 366**	**Aflibercept N = 363**
Mean change in BCVA as measured by ETDRS letter score from baseline (95% CI)	16.9 (15.7, 18.1)	17.5 (16.3, 18.6)	16.9 (15.4, 18.3)	17.3 (15.9, 18.8)
Difference in LS mean (95% CI)	-0.6 (-2.2, 1.1)		-0.4 (-2.5, 1.6)	

BCVA: Best Corrected Visual Acuity
ETDRS: Early Treatment Diabetic Retinopathy Study
CI: Confidence Interval
LS: Least Square

Figure 5: Mean Change in Visual Acuity from Baseline to Week 24 in BALATON

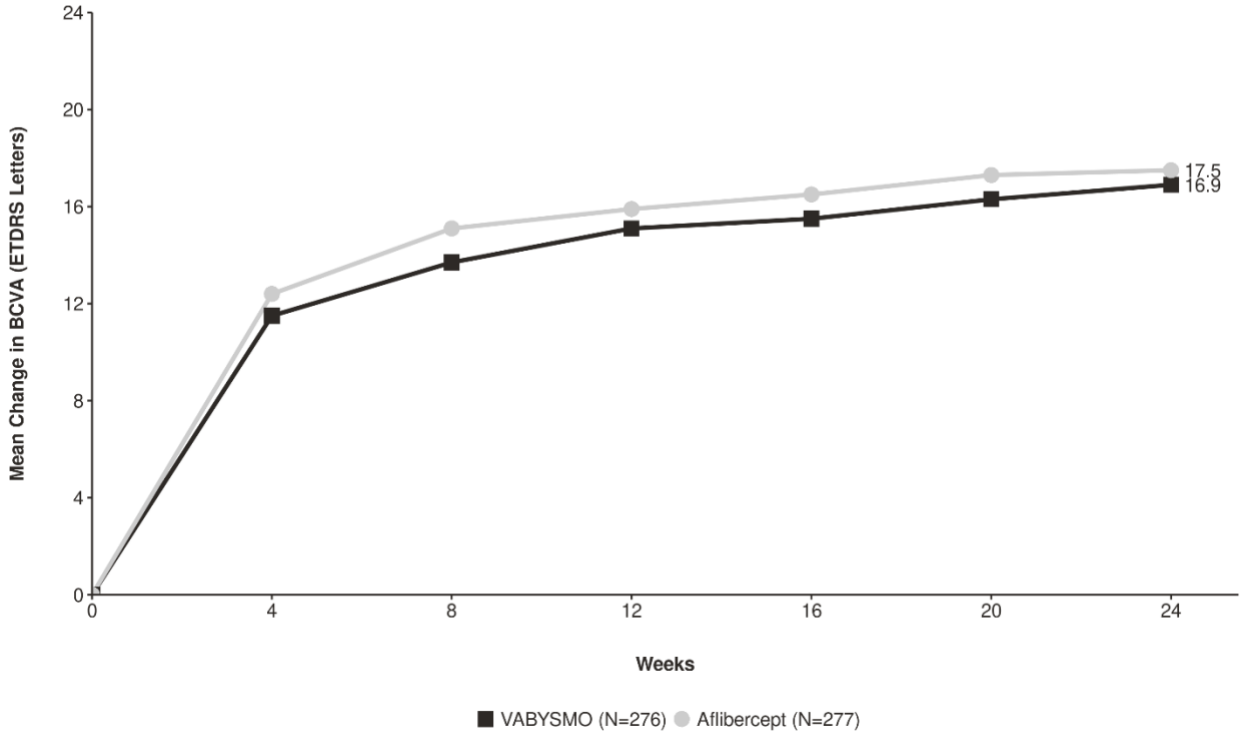
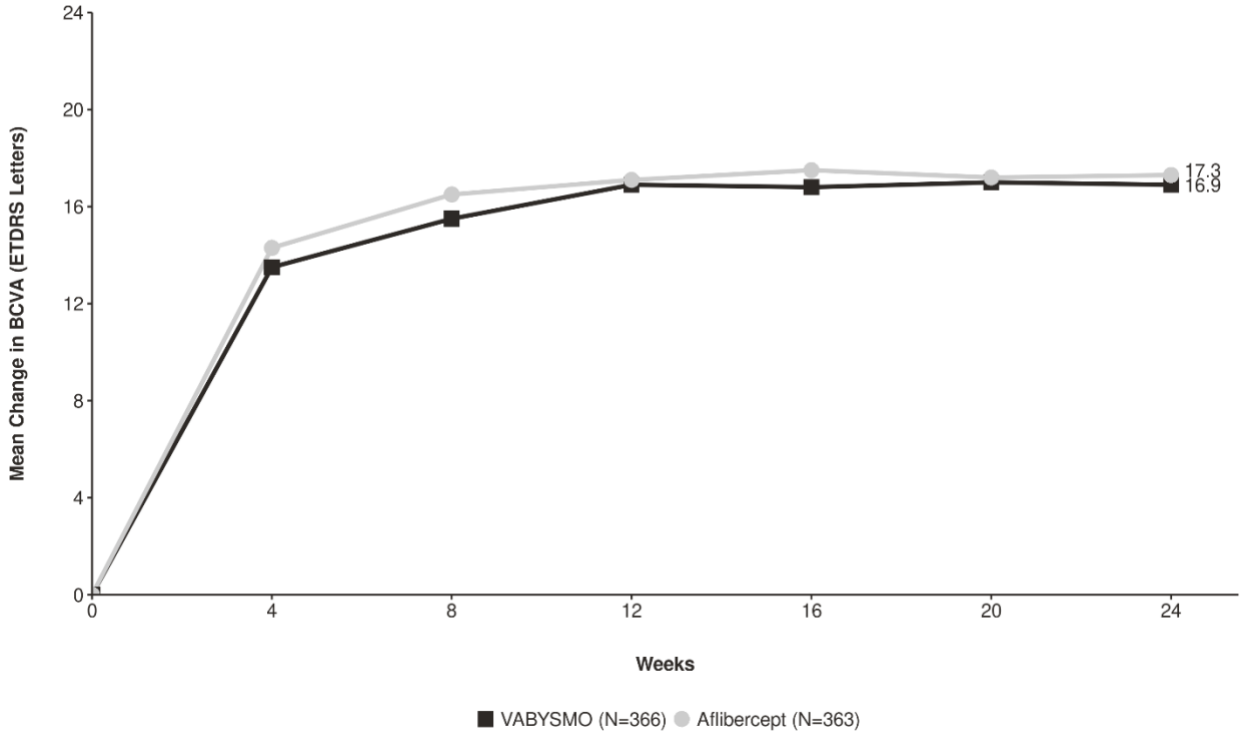


Figure 6: Mean Change in Visual Acuity from Baseline to Week 24 in COMINO



16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

VABYSMO (faricimab-svoa) injection is supplied as a clear to opalescent, colorless to brownish-yellow solution as 6 mg (0.05 mL of 120 mg/mL solution) in a single-dose prefilled syringe or single-dose vial. Each prefilled syringe or vial is for treatment of a single eye.

VABYSMO is supplied in the following presentations:

NDC NUMBER	CARTON TYPE	CARTON CONTENTS
50242-096-06	Prefilled Syringe	one 6 mg (0.05 mL of 120 mg/mL solution) single-dose prefilled glass syringe, in a sealed tray one sterile injection filter needle (30-gauge x ½ inch, 0.30 mm x 12.7 mm, Extra Thin Wall) one Prescribing Information
50242-096-01	Vial	one 6 mg (0.05 mL of 120 mg/mL solution) single-dose glass vial one sterile 5-micron blunt transfer filter needle (18-gauge x 1½ inch, 1.2 mm x 40 mm) one Prescribing Information

16.2 Storage and Handling

Store VABYSMO in the refrigerator between 2°C to 8°C (36°F to 46°F). Do not freeze. Do not shake. Keep the sealed tray containing the prefilled syringe or the vial in the original carton to protect from light.

Prior to use, the unopened prefilled syringe or glass vial of VABYSMO may be kept at room temperature, 20°C to 25°C (68°F to 77°F), for up to 24 hours. Ensure that the injection is given immediately after preparation of the dose.

17 PATIENT COUNSELING INFORMATION

Advise patients that in the days following VABYSMO administration, patients are at risk of developing endophthalmitis, retinal detachment, intraocular inflammation and retinal vasculitis with or without retinal vascular occlusion. If the eye becomes red, sensitive to light, painful, or develops a change in vision, advise the patient to seek immediate care from an ophthalmologist *[see Warnings and Precautions (5)]*.

Patients may experience temporary visual disturbances after an intravitreal injection with VABYSMO and the associated eye examinations *[see Adverse Reactions (6)]*. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

VABYSMO® [faricimab-svoa]
Manufactured by:
Genentech, Inc.
A Member of the Roche Group
1 DNA Way
South San Francisco, CA 94080-4990
U.S. License No.: 1048