

Sample Appeal Letter for SUSVIMO™ (ranibizumab injection)

Some Key Reminders:

- You may use an appeal letter for a claim (when reimbursement for a claim is underpaid or denied) or when a prior authorization is denied
 - Please indicate the type of appeal and the level of appeal for which you are filing
 - Include the appropriate ICD-10-CM diagnosis code(s)
 - Please ensure the treating physician signs the letter
-

[Date]

[Payer name]

ATTN: APPEALS

[Payer contact name]

[Payer address]

[City, State ZIP]

Re: Denial for SUSVIMO™ (ranibizumab injection)

Patient: [Patient's first and last name]

Date of Birth: [MM/DD/YYYY]

Subscriber ID #: [Insurance ID #]

Subscriber Group #: [Insurance group #]

Case ID Number: [Case ID Number (if available)]

Dates of Service: [Include all denied dates of service]

Dear [Appeals Reviewer],

I am writing to request [a/an] [indicate level of appeal: 1st, 2nd, etc.] [appeal/redetermination/reconsideration] of the above on behalf of my patient, [Patient's first and last name]. I understand from your letter that the [claim/reimbursement] was [denied/underpaid] based on [denial reason(s)]. I would like to address [the reason/those reasons] now. I would appreciate prompt review of the enclosed information demonstrating medical necessity and coverage of SUSVIMO™ (ranibizumab injection).

or

I am writing to request [a/an] [indicate level of appeal: 1st, 2nd, etc.] [appeal/redetermination/reconsideration] of the above on behalf of my patient, [Patient's first and last name]. I acknowledge your health plan's policy and I understand from your prior authorization denial letter that the denials were based on [denial reason(s)]. I would like to address [the reason/those reasons] now. I would appreciate prompt review of the enclosed information demonstrating medical necessity and coverage of SUSVIMO™ (ranibizumab injection).

Patient's Clinical History

[Patient's first and last name] is [a/an] [age]-year-old [male/female/transgender/etc.] who was diagnosed on [date] with neovascular (wet) age-related macular degeneration (AMD) and has previously responded to at least two intravitreal injections of a vascular endothelial growth factor inhibitor medication.

- [Include diagnosis and dates]
- [ICD-10-CM diagnosis codes]
- [Any past treatments]
- [Any test results that indicate failure of past treatment(s)]
- [Extenuating circumstances that would preclude alternatives to SUSVIMO]
- [Social and family information]

[REMINDER: If a payer has a published policy, include here.]

[REMINDER: If state statute exists, include here.]

Treatment Plan

[Include plan of treatment (dosage, length of treatment), FDA approval letter, relevant journal articles, clinical studies, and clinical practice guidelines that support the use of SUSVIMO. Consider mentioning experts in the field who also support the treatment.]

Summary

In summary, I am requesting [a/an] [appeal/redetermination/reconsideration] of the denial(s) of SUSVIMO therapy for my patient, [Patient's first and last name]. My patient was diagnosed with neovascular (wet) age-related macular degeneration (AMD) and has previously responded to at least two intravitreal injections of a vascular endothelial growth factor inhibitor medication. I am requesting that you reconsider coverage based on the information above. I am readily available at my office phone [Physician phone number] or via email at [Physician email] to address any questions or concerns you might have regarding this appeal. Thank you for your time and consideration.

Sincerely,

[Physician's name, credentials and signature]

Enclosures

List enclosures, which may include:

- SUSVIMO prescribing information
- Clinical notes/medical records
- Diagnostic test results
- Relevant peer-reviewed articles
- FDA approval letter for SUSVIMO
- Scans/imaging showing progressive disease
- Pathology reports, if relevant

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use SUSVIMO safely and effectively. See full prescribing information for SUSVIMO.

SUSVIMO™ (ranibizumab injection) for intravitreal use via SUSVIMO ocular implant
Initial U.S. Approval: 2006

WARNING: ENDOPHTHALMITIS
See full prescribing information for complete boxed warning.

The SUSVIMO implant has been associated with a 3-fold higher rate of endophthalmitis than monthly intravitreal injections of ranibizumab. In clinical trials, 2.0% of patients receiving an implant experienced an episode of endophthalmitis.

-----**RECENT MAJOR CHANGES**-----

Dosage and Administration (2.4, 2.7) 4/2022
Warnings and Precautions (5.4) 4/2022

-----**INDICATIONS AND USAGE**-----

SUSVIMO (ranibizumab injection), a vascular endothelial growth factor (VEGF) inhibitor, is indicated for the treatment of patients with Neovascular (wet) Age-related Macular Degeneration (AMD) who have previously responded to at least two intravitreal injections of a VEGF inhibitor (1.0).

-----**DOSAGE AND ADMINISTRATION**-----

- For intravitreal use via SUSVIMO ocular implant. (2.1)
- The recommended dose of SUSVIMO (ranibizumab injection) is 2 mg (0.02 mL of 100 mg/mL solution) continuously delivered via the SUSVIMO implant with refills every 24 weeks (approximately 6 months). (2.2)
- Supplemental treatment with 0.5 mg intravitreal ranibizumab injection may be administered in the affected eye if clinically necessary. (2.3)
- Perform the initial implantation, refill-exchange, and implant removal (if necessary) procedures under strict aseptic conditions. (2.4, 2.5, 2.6, 2.7)

-----**DOSAGE FORMS AND STRENGTHS**-----

Injection: 100 mg/mL solution in a single-dose vial (3)

-----**CONTRAINDICATIONS**-----

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

-----**WARNINGS AND PRECAUTIONS**-----

- The SUSVIMO implant and/or implant-related procedures have been associated with endophthalmitis, rhegmatogenous retinal detachment, implant dislocation, septum dislodgement, vitreous hemorrhage, conjunctival retraction, conjunctival erosion, and conjunctival bleb. Patients should be instructed to report signs or symptoms that could be associated with these events without delay. Additional surgical and/or medical management may be required. (5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7)
- **Vitreous Hemorrhage:** Temporarily discontinue antithrombotic medication prior to the implant insertion procedure to reduce the risk of vitreous hemorrhage. Vitrectomy may be needed. (5.5)
- **Postoperative Decrease in Visual Acuity:** A decrease in visual acuity usually occurs over the first two postoperative months. (5.8)

-----**ADVERSE REACTIONS**-----

The most common adverse reactions were conjunctival hemorrhage (72%), conjunctival hyperemia (26%), iritis (23%) and eye pain (10%) (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 and Medication Guide.

Revised: 4/2022

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FULL PRESCRIBING INFORMATION

WARNING: ENDOPHTHALMITIS

The SUSVIMO implant has been associated with a 3-fold higher rate of endophthalmitis than monthly intravitreal injections of ranibizumab. Many of these events were associated with conjunctival retractions or erosions. Appropriate conjunctiva management and early detection with surgical repair of conjunctival retractions or erosions may reduce the risk of endophthalmitis. In clinical trials, 2.0% of patients receiving a ranibizumab implant experienced at least one episode of endophthalmitis [see *Contraindications (4.1), Warnings and Precautions (5.1)*].

1 INDICATIONS AND USAGE

SUSVIMO (ranibizumab injection) is indicated for the treatment of patients with Neovascular (wet) Age-related Macular Degeneration (AMD) who have previously responded to at least two intravitreal injections of a Vascular Endothelial Growth Factor (VEGF) inhibitor medication.

2 DOSAGE AND ADMINISTRATION

2.1 General Information

For Intravitreal Use via SUSVIMO ocular implant.

The SUSVIMO initial fill and ocular implant insertion and implant removal procedures must be performed under aseptic conditions by a physician experienced in vitreoretinal surgery. The SUSVIMO ocular implant must be surgically implanted in the eye or removed from the eye (if medically necessary) in an operating room using aseptic technique. See SUSVIMO Instructions for Use and the standardized steps to optimize surgical outcomes.

SUSVIMO refill-exchange procedures must be performed under aseptic conditions by a physician experienced in ophthalmic surgery [see *Dosage and Administration (2.7)*].

Do not administer SUSVIMO (ranibizumab injection) as a bolus intravitreal injection. Do not substitute SUSVIMO (ranibizumab injection) with other ranibizumab products.

Initial Fill: One SUSVIMO initial fill needle (34-gauge, with integrated 5 µm filter and blue cap) is included. A 5-micron sterile filter needle (19-gauge x 1½ inch), and a 1 mL Luer lock syringe are needed but **not included**.

Refill-Exchange: One SUSVIMO refill needle (34-gauge with integrated 5 µm filter and clear cap) is included. A 5-micron sterile filter needle (19-gauge x 1½ inch), and a 1 mL Luer lock syringe are needed but **not included**.

2.2 Neovascular (Wet) Age-Related Macular Degeneration (AMD)

The recommended dose of SUSVIMO (ranibizumab injection) is 2 mg (0.02 mL of 100 mg/mL solution) continuously delivered via the SUSVIMO ocular implant with refills administered every 24 weeks (approximately 6 months).

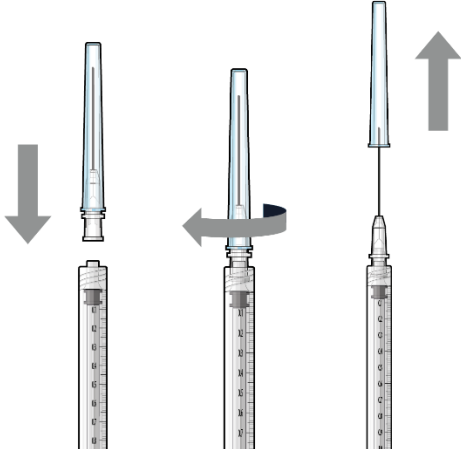
2.3 Supplemental Treatment with Intravitreal Ranibizumab Injection

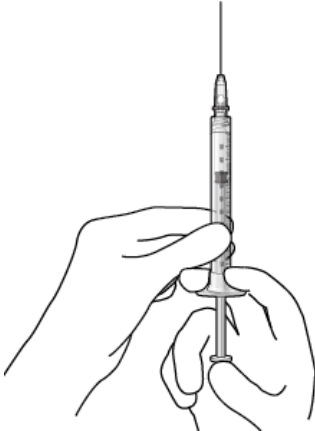
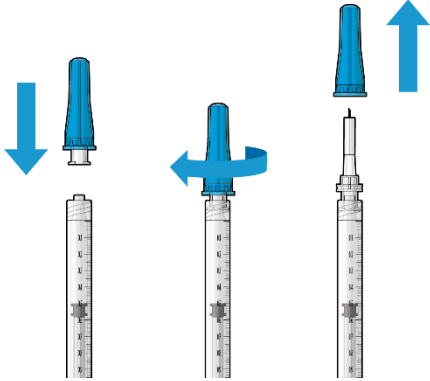
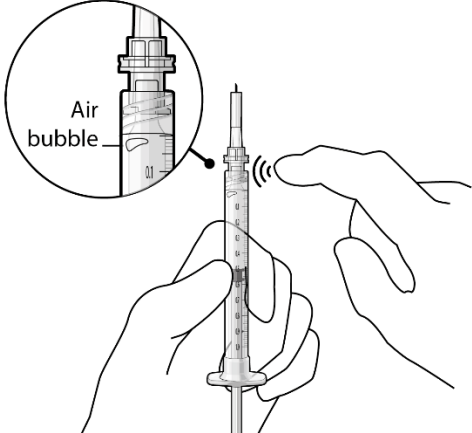
Supplemental treatment with 0.5 mg (0.05 mL of 10 mg/mL) intravitreal ranibizumab injection may be administered in the affected eye while the SUSVIMO implant is in place and if clinically necessary [see *Clinical Studies (14)*].

2.4 Ocular Implant Initial Fill

The implant initial fill procedure must be performed by a physician experienced in vitreoretinal surgery [see *Dosage and Administration (2.1)*]. The implant will be filled using aseptic technique with 0.02 mL of SUSVIMO (ranibizumab injection) prior to insertion of the implant into the patient's eye [see *Dosage and Administration (2.5)*]. Refer to the complete SUSVIMO Instructions for Use for the initial fill and implant procedure included in the insertion tool assembly carton for further details.

Use aseptic technique to carry out the following preparation steps prior to insertion of the ocular implant into the patient's eye:

| | |
|---|---|
| <p>Step 1: Gather the supplies needed.</p> <ul style="list-style-type: none"> • One SUSVIMO ocular implant with insertion tool assembly (included) • One SUSVIMO initial fill needle (34-gauge with integrated 5 µm filter) with blue cap (included) • One SUSVIMO (ranibizumab injection) 100 mg/mL vial (included) • One sterile 5-micron filter needle (19-gauge x 1½ inch) (not included) • One sterile 1 mL Luer Lock syringe (not included) | |
| <p>Step 2: Transfer Dose from Vial to Syringe</p> <p>Note: Use the filter needle (not included) to withdraw SUSVIMO (ranibizumab injection) from the vial.</p> <p>Do not use the SUSVIMO initial fill needle for this step.</p> <ul style="list-style-type: none"> • Prepare SUSVIMO (ranibizumab injection) vial by removing the flip-off cap and disinfecting the rubber vial septum with alcohol. • Attach a filter needle to the syringe by screwing it tightly onto the Luer lock (see Figure 1). • Carefully remove the needle cap by pulling it straight off. • Using aseptic technique, withdraw all of the contents of the SUSVIMO (ranibizumab injection) vial through the |  <p style="text-align: center;">Figure 1</p> |

| | |
|--|---|
| <p>filter needle into the syringe.</p> | |
| <p>Step 3: Remove Air from Syringe</p> <ul style="list-style-type: none"> • With the filter needle attached, 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 (Figure 2). • Slowly push the plunger rod just until all air is expelled from the syringe and needle. <ul style="list-style-type: none"> – It is important to preserve as much drug as possible in order to completely fill the implant. • Remove and properly dispose of the filter needle after air is removed from syringe. |  <p style="text-align: center;">Figure 2</p> |
| <p>Step 4: Attach SUSVIMO Initial Fill Needle</p> <p>Do not use the filter needle to fill the implant.</p> <ul style="list-style-type: none"> • Attach the SUSVIMO initial fill needle (included) firmly onto the syringe by screwing it tightly onto the Luer lock (see Figure 3). Ensure that the initial fill needle is attached to the syringe. • Carefully remove the needle cap by pulling straight off. • Do not wipe the needle at any time. |  <p style="text-align: center;">Figure 3</p> |
| <p>Step 5: Remove Any Remaining Air from Syringe</p> <ul style="list-style-type: none"> • With the initial fill needle attached, 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 4). • Slowly push the plunger rod just until all air is expelled from the syringe and needle, and a drop of drug solution is seen at the needle tip (see Figure 5). |  <p style="text-align: center;">Figure 4</p> |

Note: It is important to preserve as much drug as possible in order to completely fill the implant.

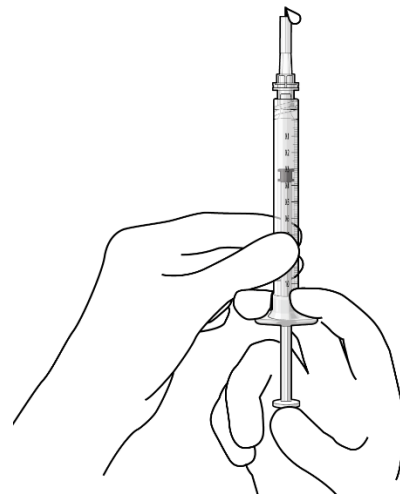


Figure 5

Step 6: Inspect the Syringe for Air Bubbles

- Inspect the syringe and the needle hub to ensure that no air bubbles are present (see Figure 6).
- If air bubbles are present, continue to remove air from the syringe and reinspect.

Note: Use the syringe within **15 minutes** of removing all air to avoid ranibizumab drying in the needle and impeding fluid flow.

Do not use the initial fill needle if the needle is clogged.

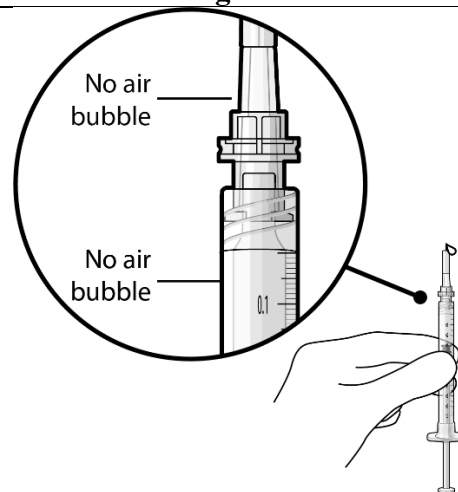


Figure 6

Step 7: Load Syringe into the Carrier

Do not hold or push on the plunger rod of the syringe while inserting the needle into the implant septum.

- Retrieve insertion tool carrier with pre-positioned implant from the inner tray.
- Align the syringe Luer lock above the Luer lock slot in the carrier to protect the needle from being damaged.
- Lower the syringe into the carrier (see Figure 7).
- Push the syringe forward until it stops, taking care to avoid touching the plunger rod (see Figure 8)
- With the syringe loaded, (see Figure 9) the initial fill needle should now be penetrating the implant septum.

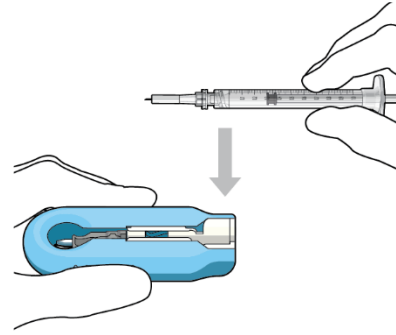


Figure 7: Align and lower the syringe into the carrier

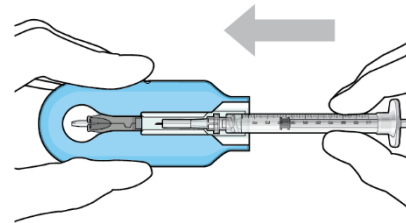


Figure 8: Push the syringe into the carrier

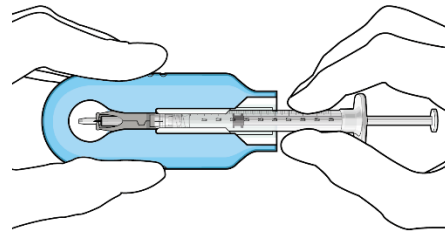


Figure 9: Syringe with initial fill needle inserted through the implant septum

Step 8: Fill Ocular Implant with SUSVIMO (ranibizumab injection) Under Microscope

- Under the microscope, **slowly** administer SUSVIMO (ranibizumab injection) into the ocular implant by slightly tilting the carrier upwards (see Figure 10).
- The ocular implant should be filled over approximately **5 to 10 seconds**, to help avoid air entrapment in the implant reservoir.

Note: When filling the ocular implant, drug solution should only exit the ocular implant from the release control element. If drug solution is leaking from the implant at a different location, such as the side of the implant, **do not** use the ocular implant. If fluid is leaking from the septum at the needle insertion site, the needle may not be fully penetrating the implant septum. Fully push the syringe forward before continuing to fill the ocular implant.

- Continue filling the ocular implant until the implant is completely full of drug solution and all air has been expelled as evidenced by a dome of drug solution formed at the tip of the implant on the release control element (see Figure 11).

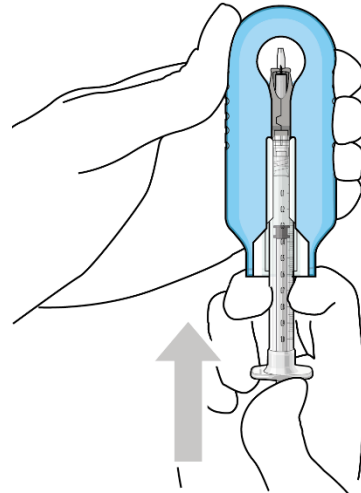


Figure 10: Administer ranibizumab into the implant

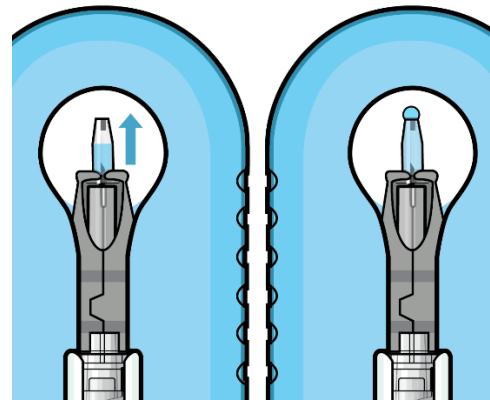


Figure 11: Dome of drug solution forms at tip of implant as viewed under magnification

Step 9: Inspect the Filled Ocular Implant Under the Microscope

- Inspect the ocular implant under the microscope to ensure that the ocular implant is completely full of drug solution (see Figure 12).

Note: Minimize air bubbles within the implant reservoir as they may cause slower drug release. If an air bubble is present, it must be no larger than 1/3 of the widest diameter of the implant. If excess air is observed, **do not** use the ocular implant.

Note: No more than 30 minutes should pass between the initial fill of the implant and the insertion into the patient's eye to ensure that the release control element remains saturated with SUSVIMO (ranibizumab injection). If SUSVIMO (ranibizumab injection) dries in the release control element, the implant may not release the drug properly into the vitreous after insertion.

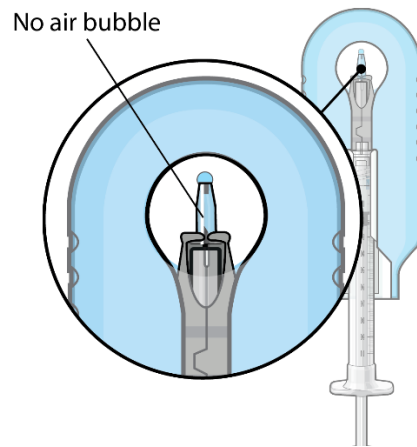


Figure 12: Proper appearance of implant after initial filling with ranibizumab

Step 10: Remove the Syringe and Guide Sleeve from the Carrier

- Remove the syringe and guide sleeve from the carrier by pulling back on the syringe (see Figure 13). The syringe will be locked into the guide sleeve.
- Properly dispose of the used syringe together with the needle and guide sleeve in a sharps disposal container or in accordance with local requirements.

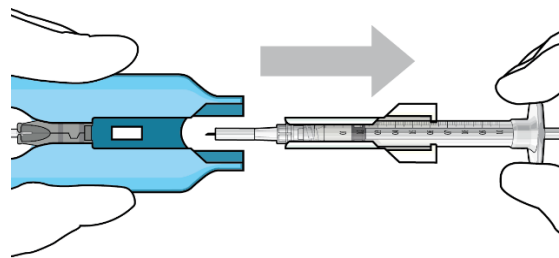


Figure 13: Remove the syringe and guide sleeve from the insertion tool carrier

Step 11: Slide the Insertion Tool Handle into the Carrier

- Slide the insertion tool handle into the guide channel of the carrier, ensuring that both components are facing upwards (see Figure 14).
- Push the handle forward as far as it will go into the gripper tips (see Figure 15).

Note: Do not withdraw the handle and implant until the eye is ready for insertion. Contact between the implant and any surface or object – even within the sterile field – may result in the introduction of a foreign body into the vitreous.

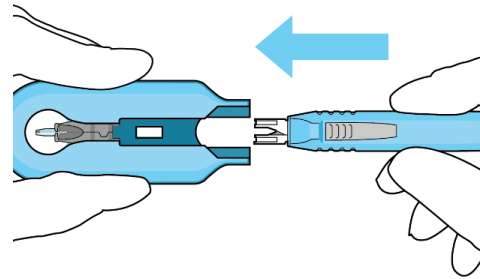


Figure 14: Insert the handle into the insertion tool carrier

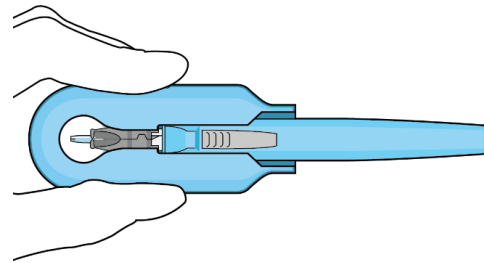


Figure 15: Fully inserted handle

2.5 Ocular Implant Insertion

SUSVIMO ocular implant insertion is a surgical procedure that is performed in an operating room. The procedure must be performed under aseptic conditions by a physician experienced in vitreoretinal surgery [see *Dosage and Administration (2.1)*].

The ocular implant is filled with SUSVIMO (ranibizumab injection) immediately prior to insertion. **No more than 30 minutes should pass between the initial fill of the ocular implant and the insertion into the patient's eye.**

After placing an infusion line in the eye, create at least a 6x6 mm peritomy of the conjunctiva and Tenon's capsule centered around the selected SUSVIMO implant location in the supero-temporal quadrant. Perform careful conjunctival incision, hemostasis of the underlying sclera, and generous undermining of Tenon's capsule. Using aseptic technique, fill the ocular implant [see *Dosage and Administration (2.4)*]. Using an MVR blade, create a full thickness dissection of the sclera 4 mm from the limbus until the pars plana is fully visible, with final target scleral incision length of 3.5 mm. Using a 532 nm laser endoprobe, apply contiguous, overlapping laser spots starting at 300 mW 1000 ms along the full length of the exposed pars plana and repeat until complete ablation is achieved. Pass a 3.2 mm slit knife perpendicularly through the center of the scleral dissection to open the underlying pars plana. Use the insertion tool to slowly insert the SUSVIMO implant into the sclero-pars plana incision perpendicular to the globe, ensuring that the long axis of the implant flange is properly aligned with the sclero-pars plana incision. Using the closed gripper tips of the insertion tool, seat the implant flush against the sclera. Clean any residual vitreous around the implant flange using a vitrector. Suture both Tenon's capsule and conjunctiva, using scleral anchoring at the apex of the peritomy,

ensuring complete coverage of the implant flange. Refer to the complete SUSVIMO Instructions for Use for the initial fill and implant procedure included in the insertion tool assembly carton for further details.

2.6 Ocular Implant Removal

Removal of the SUSVIMO ocular implant is a surgical procedure that is performed in an operating room. The procedure must be performed under aseptic conditions by a physician experienced in vitreoretinal surgery [see *Dosage and Administration (2.1)*].

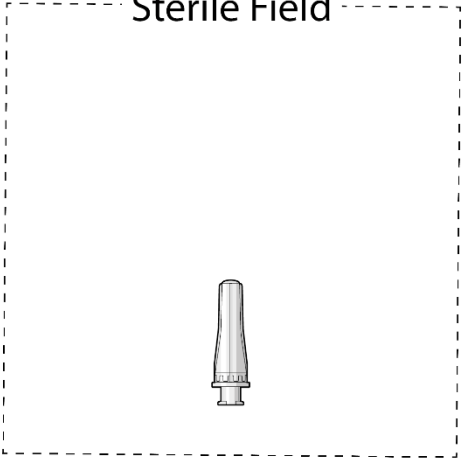
After placing an infusion line in the eye, create at least a 6x6 mm peritomy of the conjunctiva and Tenon's capsule around the SUSVIMO ocular implant flange. Remove any fibrous capsule or scar tissue that may have formed over the implant flange and septum using scalpel and forceps. With the explant tool oriented perpendicular to the globe, align the contoured tips with the long axis of the implant flange and grasp underneath the implant flange. Once the implant is secured in the explant tool, pull the implant from the eye in a perpendicular motion. Clear any vitreous prolapse present within or around the scleral wound using a vitrector. Completely close the scleral incision with multiple non-absorbable sutures. Close the Tenon's capsule and conjunctiva to completely cover the scleral incision. Refer to the complete Instructions for Use for the implant removal procedure included in the explant tool carton for further details.

2.7 Ocular Implant Refill-Exchange Procedure

The SUSVIMO ocular implant refill-exchange procedure must be performed under strict aseptic conditions by a physician experienced in ophthalmic surgery [see *Dosage and Administration (2.1)*]. This includes the use of a surgical mask, sterile gloves, and a lid speculum.

Prior to and after the refill-exchange procedure, perform a dilated slit lamp exam and/or dilated indirect ophthalmoscopy to inspect the implant in the vitreous cavity through the pupil to identify if dislodgement of the implant septum has occurred [see *Figure 31 and Warnings and Precautions (5.4)*]. If the septum has dislodged, any further refill-exchange procedures should not be performed because normal device functioning cannot be assured. Discontinue treatment with SUSVIMO (ranibizumab injection) following septum dislodgement and consider implant removal should the benefit of the removal procedure outweigh the risk.

| | |
|---|--|
| <p>Step 1: Gather the supplies needed.</p> <ul style="list-style-type: none">• One SUSVIMO Refill Needle (34-gauge with a 5 µm integrated filter) with clear cap (included)• One SUSVIMO (ranibizumab injection) 100 mg/mL vial (included)• One sterile 1 mL Luer Lock syringe (not included)• One sterile 5-micron filter needle (19-gauge x 1½ inch) (not included) | |
|---|--|

| | |
|---|--|
| <p>Additional materials required to perform the procedure but are not provided are:</p> <ul style="list-style-type: none"> • Anesthetic ophthalmic solutions • Ophthalmic broad-spectrum microbicide solution • Cotton tips and gauze • Sterile powder free gloves • Face masks • Lid speculum • Magnification such as visor or loupes • Task lighting • Indirect ophthalmoscope and lens • Sterile drape (<i>optional for refill-exchange procedure</i>) | |
| <p>Step 2: Inspect Packaging and Components</p> <ul style="list-style-type: none"> • Prior to use in the clinic, inspect the packaging of the components for damage. Do not use if the sterility has been compromised or the contents have been dropped, damaged, or tampered with. • Check the expiration date printed on the label. • Remove the vial from the carton. <u>Note</u>: the outside of the vial is not sterile. • Use aseptic technique to open packaging and remove the sterile refill needle from the tray. • Inspect components and place onto sterile field (see Figure 16). | <p style="text-align: center;">Sterile Field</p>  <p style="text-align: center;">Figure 16</p> |
| <p>Step 3: Inspect SUSVIMO (ranibizumab injection)</p> <ul style="list-style-type: none"> • Visually inspect the contents of the SUSVIMO (ranibizumab injection) vial for particulate matter and discoloration. • SUSVIMO should be colorless to pale brown <p>Do not use if particulate, cloudiness, or discoloration are visible.</p> | |

Step 4: Patient Preparation

- Dilate the pupil of the eye.
- Perform slit lamp examination and/or indirect ophthalmoscopy to inspect the implant and its components in the vitreous cavity through the dilated pupil.
- Position the patient on exam chair in the supine position at approximately 20° to 30° angle for optimal visualization of the implant.
- Apply a broad-spectrum microbicide to the periocular skin, eyelid, and ocular surface prior to the refill-exchange procedure. The use of a sterile drape is up to the physician's discretion.
- Perform the procedure under topical anesthesia.
- If needed, subconjunctival anesthesia may be administered in the nasal quadrant, away from the implant.

Step 5: Transfer Dose from Vial to Syringe

Note: Use the filter needle to withdraw SUSVIMO (ranibizumab injection) from the vial.

Do not use the SUSVIMO refill needle for this step.

- Prepare ranibizumab vial by removing the flip-off cap and disinfecting the rubber vial septum with alcohol.
- Attach a filter needle to the syringe by screwing it tightly onto the Luer lock (see Figure 17).
- Carefully remove the needle cap by pulling it straight off.
- Using aseptic technique, withdraw all of the contents of the SUSVIMO

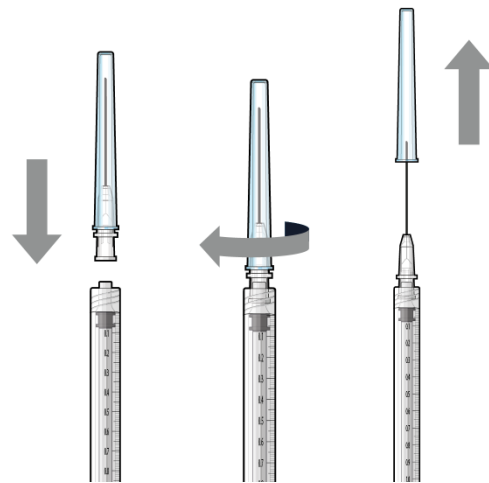
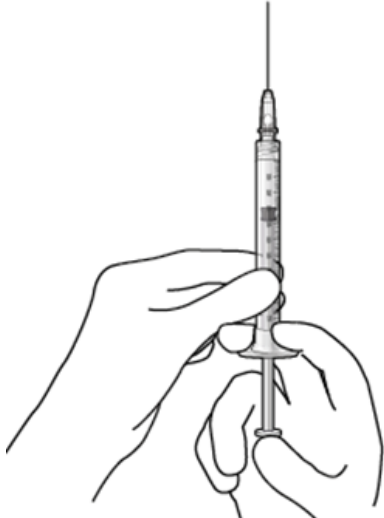
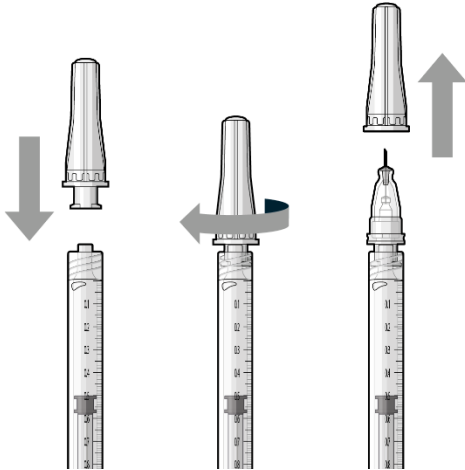


Figure 17

| | |
|--|--|
| <p>(ranibizumab injection) vial through the filter needle into the syringe.</p> | |
| <p>Step 6: Remove Air from Syringe</p> <ul style="list-style-type: none"> • With the filter needle attached, 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 (Figure 18). • Slowly push the plunger rod just until the air is expelled from the syringe and needle. <ul style="list-style-type: none"> – It is important to preserve as much drug as possible in order to completely refill the implant • Remove and properly dispose of the filter needle after air is removed from the syringe. |  <p style="text-align: center;">Figure 18</p> |
| <p>Step 7: Attach SUSVIMO Refill Needle</p> <p>Do not use the filter needle to fill the implant.</p> <ul style="list-style-type: none"> • Attach the SUSVIMO refill needle firmly onto the syringe by screwing it tightly onto the Luer lock (see Figure 19). Ensure that the refill needle is attached to the syringe. • Carefully remove the needle cap, pulling straight off to avoid damage to the needle cannula. • Do not wipe the needle at any time. |  <p style="text-align: center;">Figure 19</p> |

Step 8: Remove Any Remaining Air from Syringe and Adjust Drug Dose

- With the refill needle attached, 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 20).
- Slowly push the plunger rod until all air is expelled from the syringe and needle and the uppermost edge of the black plunger tip is aligned with the **0.1 mL** dose mark (see Figure 21).

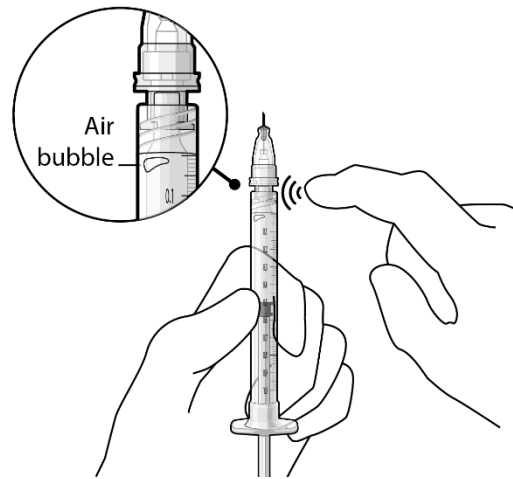


Figure 20

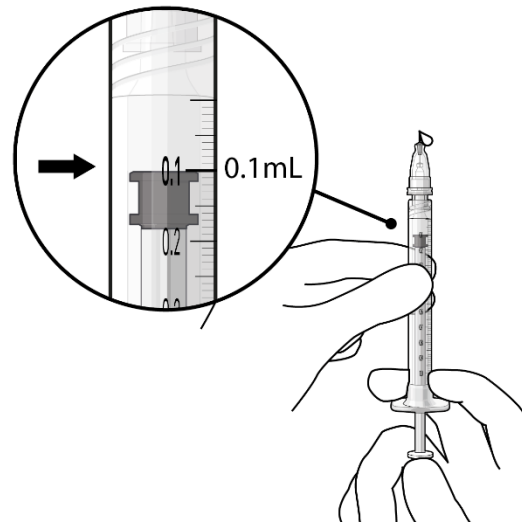


Figure 21

Step 9: Inspect the Syringe for Air Bubbles

Note: Ensure no air bubbles are present in the syringe and needle hub. Air injected into the implant could result in slower drug release.

- Inspect the syringe and the needle hub using magnification to ensure that no air bubbles are present (see Figure 22).

Note: Use the syringe within **15 minutes** of removing all air and adjusting the drug

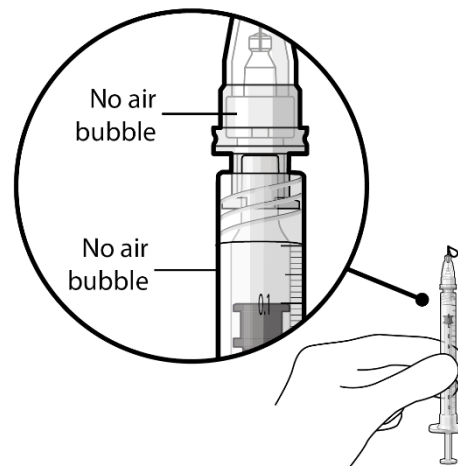


Figure 22

dose to avoid drug solution drying in the needle and impeding fluid flow.

Do not use the refill needle or syringe if the needle is clogged.

Step 10: Stabilize the globe and orient the refill needle

Note: Perform the refill-exchange procedure using magnification (e.g., loupes, reading glasses, magnifiers) for visual assistance.

- After placing the lid speculum in the eye, stabilize the globe with a cotton-tipped applicator to minimize eye movement (see Figure 23).
 - Recommend standing on the contralateral side of the implanted eye, with the patient looking down and toward their nose to optimally expose the implant.
- Orient the refill needle perpendicular to the globe (see Figure 24).

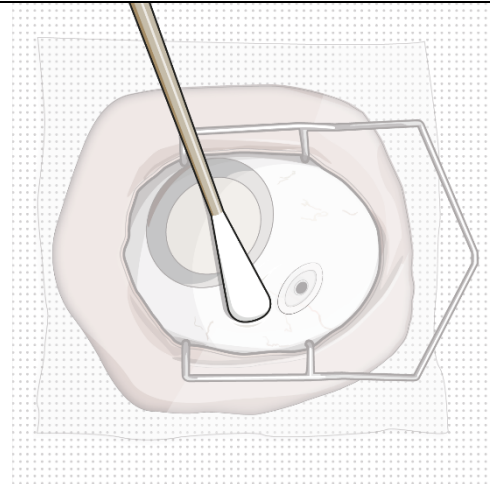


Figure 23

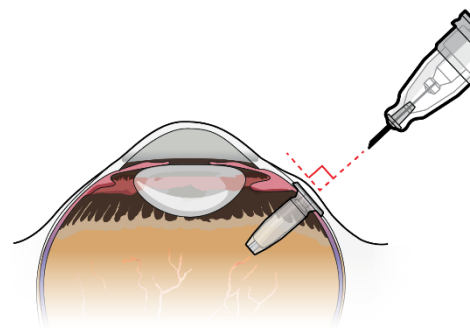


Figure 24

Step 11: Insert the Refill Needle

Note: Insert needle at the very center of the implant septum and perpendicular to the implant to ensure the needle inserts fully. **Do not** maneuver if there is resistance as it will bend the needle.

Do not use a bent refill needle; replace if bent or if damage is suspected.

- Targeting the center of the implant septum, insert the refill needle perpendicularly through the conjunctiva and into the implant septum (see Figure 25).
 - If excessive resistance, withdraw the refill needle. Orient and insert again.
 - **Do not** twist when encountering conjunctiva and Tenon’s capsule to gain access to the septum, as damage to the overlying tissue and to the septum of the device may result.
- Continue inserting the needle until the soft stop of the refill needle makes physical contact with the conjunctiva (see Figure 26) to provide a tactile cue that optimal contact has been made.

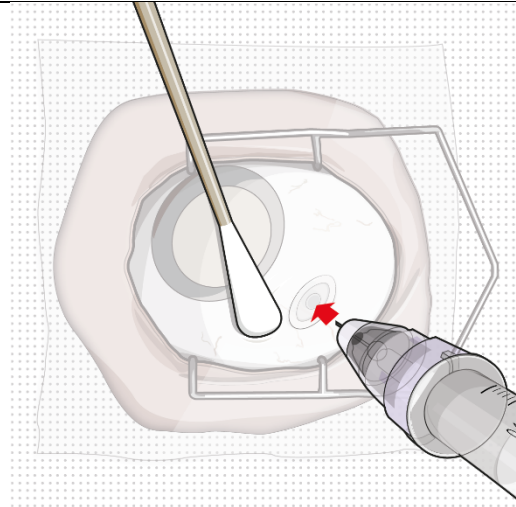


Figure 25

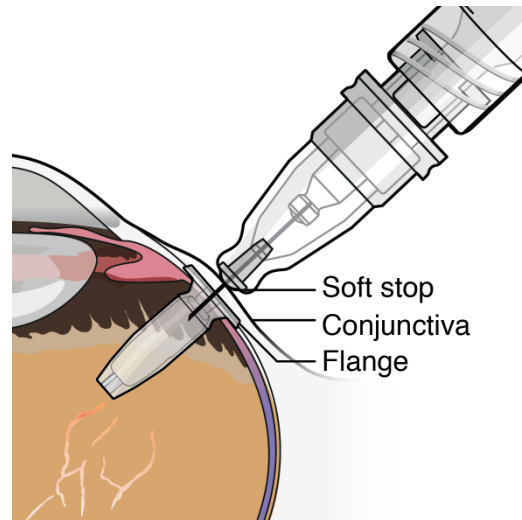


Figure 26

Step 12: Refill the SUSVIMO Implant

- Refill the implant **slowly**, by delivering the entire contents of the syringe into the implant, over approximately **5 to 10 seconds**, to avoid pressure build-up in the implant reservoir. The soft stop of the refill needle must remain in contact with the conjunctiva throughout the procedure.
- As ranibizumab is administered into the implant, existing solution from the implant should immediately begin to fill the refill needle fluid collection chamber (see Figure 27).

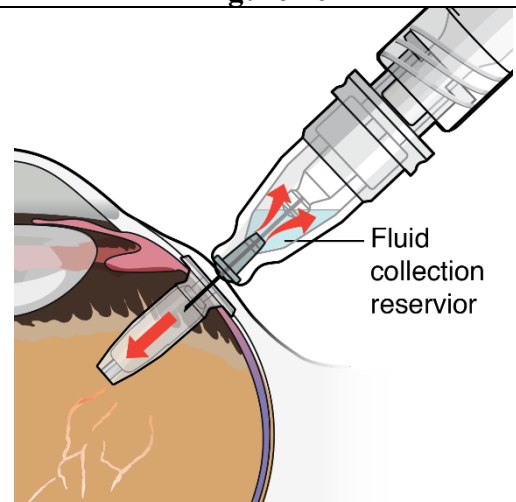
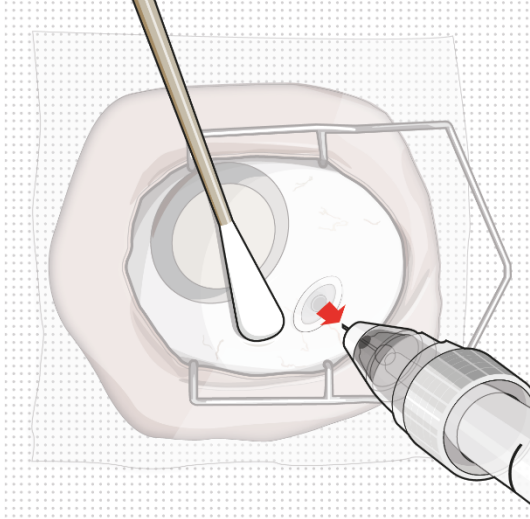


Figure 27

| | |
|--|---|
| <ul style="list-style-type: none"> • If fluid is not observed collecting in the refill needle fluid collection reservoir, stop injecting and ensure the refill needle is inserted into the center of the implant septum at a perpendicular angle and the soft stop is in contact with the conjunctiva. • Administer all of the syringe contents in order to achieve the target replacement ranibizumab concentration in the implant reservoir. | |
| <p>Step 13: Withdraw the Syringe</p> <ul style="list-style-type: none"> • Withdraw the syringe perpendicular to the globe to avoid damaging the septum (see Figure 28). • A cotton-tipped applicator may be used to provide counter traction to the conjunctiva during needle withdrawal. |  <p style="text-align: center;">Figure 28</p> |
| <p>Step 14: Dispose of the Used Components</p> <ul style="list-style-type: none"> • Do not recap the needle or detach it from the syringe. Dispose of the used syringe together with the refill needle in a sharps disposal container or in accordance with local requirements. | |
| <p>Step 15: Perform Indirect Ophthalmoscopy</p> <ul style="list-style-type: none"> • Perform dilated indirect ophthalmoscopy (and slit lamp exam as needed) to ensure continued proper position of the implant and its components (e.g., septum) in the vitreous cavity and to examine for complications. | |

2.8 Delayed or Missed Doses

If a planned dose (refill-exchange) of SUSVIMO (ranibizumab injection) is missed, it should be administered as soon as possible and the subsequent refill-exchange procedures should be performed 24 weeks (approximately 6 months) thereafter.

2.9 Dosage (Refill-Exchange) Modifications for Adverse Reactions

Table 1 describes dosage modifications for specific adverse Reactions [see *Warnings and Precautions (5)*]. No dosage reductions for SUSVIMO are recommended.

Table 1: Dosage (Refill-Exchange) Modifications for Adverse Reactions

| Adverse Reactions | Dosage Modification |
|--|--|
| Intraocular inflammation \geq 1 + cells or flare | Withhold dose (refill-exchange) |
| Sight threatening events (e.g., rhegmatogenous retinal detachment, vitreous hemorrhage, unexplained vision loss, etc.) | Withhold dose (refill-exchange) |
| Local infections of either eye | Withhold dose (refill-exchange) |
| Infectious endophthalmitis | Withhold dose (refill-exchange) |
| Severe systemic infection | Withhold dose (refill-exchange) |
| Observed damage to the implant | Withhold dose (refill-exchange) and consider SUSVIMO implant removal [see <i>Dosage and Administration (2.6, 2.7)</i>]. |

3 DOSAGE FORMS AND STRENGTHS

Injection: 100 mg/mL, clear to slightly opalescent, colorless to pale brown solution in a single-dose vial

4 CONTRAINDICATIONS

4.1 Ocular or Periocular Infections

SUSVIMO (ranibizumab injection) is contraindicated in patients with ocular or periocular infections.

4.2 Active Intraocular Inflammation

SUSVIMO (ranibizumab injection) is contraindicated in patients with active intraocular inflammation.

4.3 Hypersensitivity

SUSVIMO (ranibizumab injection) is contraindicated in patients with known hypersensitivity to ranibizumab products or any of the excipients in SUSVIMO (ranibizumab injection).

5 WARNINGS AND PRECAUTIONS

The SUSVIMO implant and/or implant-related procedures have been associated with endophthalmitis, rhegmatogenous retinal detachment, implant dislocation, septum dislodgement, vitreous hemorrhage, conjunctival erosion, conjunctival retraction, and conjunctival blebs. Patients should be instructed to report any signs or symptoms that could be associated with these events without delay. In some cases, these events can present asymptotically. The implant and the tissue overlying the implant flange should be monitored routinely following the implant insertion, and refill-exchange procedures to permit early medical or surgical intervention as necessary. Special precautions need to be taken when handling SUSVIMO components [see *How Supplied/Storage and Handling (16.3)*].

5.1 Endophthalmitis

In the active comparator period of controlled clinical trials, the ranibizumab implant has been associated with a 3-fold higher rate of endophthalmitis than monthly intravitreal injections of ranibizumab (1.7% in the SUSVIMO arm vs 0.5% in the intravitreal arm). When including extension phases of clinical trials, 2.0% (11/555) of patients receiving the ranibizumab implant experienced an episode of endophthalmitis. Reports occurred between days 5 and 853, with a median of 173 days. Many, but not all, of the cases of endophthalmitis reported a preceding or concurrent conjunctival retraction or erosion event.

Endophthalmitis should be treated promptly in an effort to reduce the risk of vision loss and maximize recovery. The SUSVIMO (ranibizumab injection) dose (refill-exchange) should be delayed until resolution of endophthalmitis [*see Dosage and Administration (2.9) and Adverse Reactions (6.1)*].

Patients should not have an active or suspected ocular or periocular infection or severe systemic infection at the time of any SUSVIMO implant or refill procedure. Appropriate intraoperative handling followed by secure closure of the conjunctiva and Tenon's capsule, and early detection and surgical repair of conjunctival erosions or retractions may reduce the risk of endophthalmitis [*see Warnings and Precautions (5.5)*].

5.2 Rhegmatogenous Retinal Detachment

Rhegmatogenous retinal detachments have occurred in clinical trials of SUSVIMO and may result in vision loss. Rhegmatogenous retinal detachments should be promptly treated with an intervention (e.g., pneumatic retinopexy, vitrectomy, or laser photocoagulation). SUSVIMO (ranibizumab injection) dose (refill-exchange) should be delayed in the presence of a retinal detachment or retinal break [*see Dosage and Administration (2.9)*].

Careful evaluation of the retinal periphery is recommended to be performed, and any suspected areas of abnormal vitreo-retinal adhesion or retinal breaks should be treated before inserting the implant in the eye.

5.3 Implant Dislocation

In clinical trials, the device has dislocated/subluxated into the vitreous cavity or has extended outside the vitreous cavity into or beyond the subconjunctival space. Device dislocation requires urgent surgical intervention. Strict adherence to the scleral incision length and appropriate targeting of the pars plana during laser ablation may reduce the risk of implant dislocation.

5.4 Septum Dislodgement

In clinical trials, a type of implant damage where the septum has dislodged into the implant body has been reported. Perform a dilated slit lamp exam and/or dilated indirect ophthalmoscopy to inspect the implant in the vitreous cavity through the pupil prior to and after the refill-exchange procedure to identify if septum dislodgement has occurred. Discontinue treatment with SUSVIMO (ranibizumab injection) following septum dislodgement and consider implant removal should the benefit of the removal procedure outweigh the risk [*see Dosage and Administration (2.8)*].

Appropriate handling and insertion of the refill needle into the septum (avoid twisting and/or rotation) is required to minimize the risk of septum dislodgement [*see Dosage and Administration (2.7)*].

5.5 Vitreous Hemorrhage

Vitreous hemorrhages may result in temporary vision loss. Vitrectomy may be needed in the case of a non-clearing vitreous hemorrhage [*see Dosage and Administration (2.9)*].

In clinical trials of SUSVIMO including extension phases, vitreous hemorrhages were reported in 5.2% (23/443) of patients receiving SUSVIMO. The majority of these hemorrhages occurred within the first post-operative month following surgical implantation and the majority of vitreous hemorrhages resolved spontaneously. Patients on antithrombotic medication (e.g., oral anticoagulants, aspirin, nonsteroidal anti-inflammatory drugs) may be at increased risk of vitreous hemorrhage. Antithrombotic medications are recommended to be temporarily interrupted prior to the implant insertion procedure. The SUSVIMO (ranibizumab injection) dose (refill-exchange) should be delayed in the event of sight-threatening vitreous hemorrhage. The use of pars plana laser ablation and scleral cauterization should be performed to reduce the risk of vitreous hemorrhage.

5.6 Conjunctival Erosion or Retraction

A conjunctival erosion is a full thickness degradation or breakdown of the conjunctiva in the area of the implant flange. A conjunctival retraction is a recession or opening of the limbal and/or radial peritomy. Conjunctival erosions or retractions have been associated with an increased risk of endophthalmitis, especially if the implant becomes exposed. Surgical intervention (e.g., conjunctival/Tenon's capsule repair) is recommended to be performed in case of conjunctival erosion or retraction with or without exposure of the implant flange.

In clinical trials of SUSVIMO including extension phases, 3.6% (16/443) of patients receiving SUSVIMO reported conjunctival erosion and 1.6% (7/443) of patients receiving SUSVIMO reported conjunctival retraction in the study eye.

Appropriate intraoperative handling of conjunctiva and Tenon's capsule to preserve tissue integrity and secure closure of peritomy while ensuring placement of sutures away from implant edge may reduce the risk of conjunctival erosion or retraction. The implant and the tissue overlying the implant flange should be monitored routinely following the implant insertion.

5.7 Conjunctival Bleb

A conjunctival bleb is an encapsulated elevation of the conjunctiva above the implant flange, which may be secondary to subconjunctival thickening or fluid. Conjunctival blebs may require surgical management to avoid further complications, especially if the implant septum is no longer identifiable due to the conjunctival bleb.

In clinical trials of SUSVIMO including extension phases, 5.9% (26/443) of patients receiving SUSVIMO reported conjunctival bleb/conjunctival filtering bleb leak in the study eye. Strict adherence to the scleral incision length, appropriate intraoperative handling of conjunctiva and Tenon's capsule to preserve tissue integrity and secure closure of peritomy, and proper seating of

the refill needle during refill-exchange procedures may reduce the risk of conjunctival bleb.

5.8 Postoperative Decrease in Visual Acuity

Visual acuity was decreased by 4 letters on average in the first postoperative month and 2 letters on average in the second postoperative month following initial implantation of SUSVIMO [see *Clinical Studies (14)*].

5.9 Air Bubbles Causing Improper Filling of the Implant

Minimize air bubbles within the implant reservoir as they may cause slower drug release. During the initial fill procedure, if an air bubble is present, it must be no larger than 1/3 of the widest diameter of the implant. If excess air is observed after initial fill, **do not** use the implant. During the refill-exchange procedure, if excess air is present in the syringe and needle **do not** use the syringe and needle. If excess air bubbles are observed after the refill-exchange procedure, consider repeating the refill-exchange procedure.

5.10 Deflection of the Implant

Use caution when performing ophthalmic procedures that may cause deflection of the implant and subsequent injury. For example, B-scan ophthalmic ultrasound, scleral depression, or gonioscopy.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the label:

- Endophthalmitis [see *Warnings and Precautions (5.1)*]
- Rhegmatogenous Retinal Detachment [see *Warnings and Precautions (5.2)*]
- Implant Dislocation [see *Warnings and Precautions (5.3)*]
- Vitreous Hemorrhage [see *Warnings and Precautions (5.5)*]
- Conjunctival Erosion or Retraction [see *Warnings and Precautions (5.6)*]
- Conjunctival Bleb [see *Warnings and Precautions (5.7)*]
- Postoperative Decrease in Visual Acuity [see *Warnings and Precautions (5.8)*]

6.1 Clinical Trials Experience

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

The data below (Table 2) reflect exposure of 248 patients with nAMD in the Archway study following the SUSVIMO initial fill and implant insertion, refill, and implant removal (if necessary) procedures up to Week 40. In this patient population the most common ($\geq 10\%$) adverse reactions up to Week 40 were conjunctival hemorrhage (72%), conjunctival hyperemia (26%), iritis (23%), and eye pain (10%).

Table 2 Adverse Reactions in nAMD patients occurring in $\geq 4\%$ of patients in the SUSVIMO arm

| Adverse Reactions | Week 40 | |
|---|--------------------|--|
| | SUSVIMO n = 248 | Intravitreal ranibizumab n = 167 |
| Conjunctival hemorrhage | 72% | 6% |
| Conjunctival hyperemia | 26% | 2% |
| Iritis ¹ | 23% | 0.6% |
| Eye pain | 10% | 5% |
| Vitreous floaters | 9% | 2% |
| Conjunctival bleb/ filtering bleb leak ² | 9% | 0 |
| Foreign body sensation in eyes | 7% | 1% |
| Headache ³ | 7% | 2% |
| Hypotony of eye | 6% | 0 |
| Vitreous detachment | 6% | 5% |
| Vitreous hemorrhage | 5% | 2% |
| Conjunctival edema | 5% | 0 |
| Corneal disorder | 4% | 0 |
| Corneal abrasion ⁴ | 4% | 0.6% |
| Corneal edema | 4% | 0 |

¹ Iritis includes: iritis, anterior chamber flare, and anterior chamber cell

² Conjunctival bleb/filtering bleb leak includes: conjunctival bleb, conjunctival filtering bleb leak, conjunctival cyst, subconjunctival cyst, and implant site cyst

³ Headache includes: headache and procedural headache

⁴ Corneal abrasion includes: corneal abrasion and vital dye staining cornea present.

6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immune response in patients treated with ranibizumab including SUSVIMO. The detection of an immune response is highly dependent on the sensitivity, specificity, and drug tolerance level of the assay. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies in the study described below with the incidence of antibodies in other studies or to other products may be misleading.

In previously treated nAMD patients, anti-ranibizumab antibodies were detected in 2.1% (5 of 243) of patients prior to insertion of the SUSVIMO implant. After the SUSVIMO implant insertion and treatment, anti-ranibizumab antibodies developed in 12% (29 of 247) patients. No clinically meaningful differences in the pharmacokinetics, efficacy, or safety in patients with treatment-emergent anti-ranibizumab antibodies were observed.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies of SUSVIMO (ranibizumab injection) administration in pregnant women. Administration of ranibizumab to pregnant monkeys

throughout the period of organogenesis resulted in a low incidence of skeletal abnormalities at intravitreal doses up to 41 times the human exposure (based on serum levels following the recommended clinical dose). No skeletal abnormalities were observed at serum trough levels similar to the human exposure after a single eye treatment at the recommended clinical dose [*see Animal Data*].

Animal reproduction studies are not always predictive of human response, and it is not known whether ranibizumab can cause fetal harm when administered to a pregnant woman. Based on the anti-VEGF mechanism of action for ranibizumab [*see Clinical Pharmacology (12.1)*], treatment with SUSVIMO (ranibizumab injection) may pose a risk to human embryofetal development.

All pregnancies have a background risk of birth defects, 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 intravitreal injections of ranibizumab every 14 days starting on Day 20 of gestation, until Day 62 at doses of 0, 0.125, and 1 mg/eye. Skeletal abnormalities including incomplete and/or irregular ossification of bones in the skull, vertebral column, and hindlimbs and shortened supernumerary ribs were seen at a low incidence in fetuses from animals treated with 1 mg/eye of ranibizumab. The 1 mg/eye dose resulted in trough serum ranibizumab levels up to 41 times higher than observed human C_{max} levels of SUSVIMO (ranibizumab injection) after treatment of a single eye.

No skeletal abnormalities were seen at the lower dose of 0.125 mg/eye, a dose which resulted in trough exposures similar to single eye treatment with SUSVIMO (ranibizumab injection) in humans. No effect on the weight or structure of the placenta, maternal toxicity, or embryotoxicity was observed.

8.2 Lactation

Risk Summary

There are no data available on the presence of ranibizumab in human milk, the effects of ranibizumab on the breastfed infant or the effects of ranibizumab on milk production/excretion. Because many drugs are excreted in human milk, and because the potential for absorption and harm to infant growth and development exists, caution should be exercised when SUSVIMO is administered to a nursing woman.

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

8.3 Females and Males of Reproductive Potential

Contraception

Females of reproductive potential should use effective contraception during treatment with SUSVIMO (ranibizumab injection) and for at least 12 months after the last dose of SUSVIMO (ranibizumab injection).

Infertility

No studies on the effects of ranibizumab on fertility have been conducted and it is not known whether ranibizumab can affect reproduction capacity. Based on the anti-VEGF mechanism of action for ranibizumab, treatment with SUSVIMO (ranibizumab injection) may pose a risk to reproductive capacity.

8.4 Pediatric Use

The safety and efficacy of SUSVIMO (ranibizumab injection) in pediatric patients have not been established.

8.5 Geriatric Use

In the Archway study, 90% (222 of 248) of the patients randomized to treatment with SUSVIMO were ≥ 65 years old and approximately 57% (141 of 248) were ≥ 75 years old. No notable difference in treatment effect or safety was seen with increasing age.

11 DESCRIPTION

Ranibizumab is a recombinant humanized IgG1 kappa isotype monoclonal antibody fragment for intraocular use. Ranibizumab binds to and inhibits the biologic activity of human vascular endothelial growth factor-A (VEGF-A). Ranibizumab, which lacks an Fc region, has a molecular weight of approximately 48 kilodaltons and is produced by an *E. coli* expression system in a nutrient medium containing the antibiotic tetracycline. Tetracycline is not detectable in the final product.

SUSVIMO (ranibizumab injection) is supplied as a sterile, clear to slightly opalescent, colorless to pale brown solution for intravitreal use via the SUSVIMO implant. Each single-dose vial contains 10 mg of ranibizumab, histidine HCl (0.1 mg), polysorbate 20 (0.01 mg), sucrose (8.2 mg), and Water for Injection, in 0.1 mL of solution with a pH of 5.5. The SUSVIMO implant is designed to contain approximately 0.02 mL (2 mg) of ranibizumab solution when filled. SUSVIMO does not contain an antimicrobial preservative.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Ranibizumab binds to the receptor binding site of multiple biologically active forms of VEGF-A, including VEGF₁₁₀. VEGF-A has been shown to cause neovascularization and leakage in models of ocular angiogenesis and vascular occlusion and is thought to contribute to pathophysiology of neovascular AMD. The binding of ranibizumab to VEGF-A prevents the interaction of VEGF-A with its receptors (VEGFR1 and VEGFR2) on the surface of endothelial cells, reducing endothelial cell proliferation, vascular leakage, and new blood vessel formation.

12.3 Pharmacokinetics

The SUSVIMO implant provides a continuous release of ranibizumab where the release of

ranibizumab into the vitreous decreases over time as the concentration in the implant decreases with a half-life of approximately 25 weeks. The ranibizumab serum concentrations with a SUSVIMO 24-week treatment interval are maintained below the maximum and above the minimum concentrations experienced with monthly 0.5 mg intravitreal ranibizumab.

Distribution

Following implant insertion of SUSVIMO, the mean (\pm SD) maximum ranibizumab serum concentration (C_{\max}) was 0.48 (\pm 0.17) ng/mL and median (range) time to maximum serum concentration (T_{\max}) was 26 (1 – 89) days. Following the initial fill and refill of SUSVIMO in patients with AMD, maximum serum concentrations of ranibizumab were below the ranibizumab concentration necessary to inhibit the biological activity of VEGF by 50%. Ranibizumab did not accumulate in serum when administered with refills every 24 weeks.

Elimination

Metabolism

The metabolism of SUSVIMO (ranibizumab injection) has not been studied. SUSVIMO (ranibizumab injection) is a monoclonal antibody fragment and antibodies are cleared principally by catabolism.

Excretion

The full excretion profile for ranibizumab following administration of SUSVIMO is unknown.

Specific Populations

In a population pharmacokinetic analysis of AMD patients with SUSVIMO, 75% (220 of 295) had renal impairment (42% mild [CrCL 60 to 89 mL/min], 30% moderate [CrCL 30 to 59 mL/min] and 2% severe [CrCL < 30mL/min]). Systemic clearance of ranibizumab was slightly lower in renally impaired patients, but was not clinically significant. No clinically significant differences in the pharmacokinetics of ranibizumab were observed based on age.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No studies have been conducted to determine the carcinogenic or mutagenic potential of SUSVIMO (ranibizumab injection). Based on the anti-VEGF mechanism of action for ranibizumab, treatment with SUSVIMO (ranibizumab injection) may pose a risk to reproductive capacity [*see Females and Males of Reproductive Potential (8.3)*].

14 CLINICAL STUDIES

The clinical efficacy and safety of SUSVIMO (ranibizumab injection) was assessed in a randomized, visual assessor-masked, active treatment-controlled study (Archway-NCT03677934) in patients with AMD. A total of 415 patients (248 in the SUSVIMO arm and 167 in the intravitreal ranibizumab arm) were enrolled and treated in this study. Patients were diagnosed with nAMD within the 9 months prior to screening and received ≥ 3 doses of anti-VEGF intravitreal agents in the study eye within the last 6 months prior to screening. Each patient was required to have demonstrated a response to an anti-VEGF intravitreal agent prior to randomization. Patients were randomized in a 3:2 ratio to receive continuous delivery of SUSVIMO (ranibizumab injection) via the SUSVIMO implant every 24

weeks or 0.5 mg intravitreal ranibizumab injections every 4 weeks. For patients randomized to the SUSVIMO arm, supplemental treatment with 0.5 mg intravitreal ranibizumab injections was available at Weeks 16, 20, 40, 44, 64, 68, 88, and 92, if needed. In the first 24 weeks, 1.6% of patients assessed for supplemental treatment received 1 or more supplemental treatment(s) and in the following 24 weeks, 5.4% of patients assessed for supplemental treatment received 1 or more supplemental treatment(s).

The primary efficacy endpoint of change from baseline in distance Best Corrected Visual Acuity (BCVA) score averaged over Week 36 and Week 40 demonstrated that SUSVIMO was equivalent to intravitreal ranibizumab injections administered every 4 weeks. Detailed efficacy results are shown in Table 3 and Figure 29 below.

Table 3 Visual Acuity outcomes at Week 40 in Archway (GR40548) Study

| Outcome Measure* | SUSVIMO (100 mg/mL) n=248 | Intravitreal ranibizumab 0.5 mg (10 mg/mL) n=167 | Difference (95% CI)** |
|--|--|---|----------------------------------|
| Adjusted Mean change from baseline in BCVA score averaged over Weeks 36 and 40 | 0.2 | 0.5 | -0.3 (-1.7, 1.1)*** |

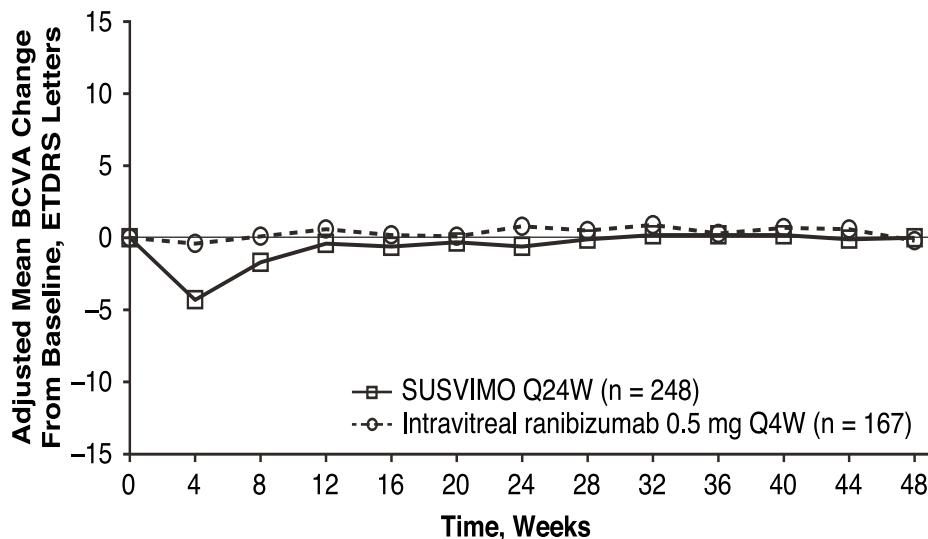
BCVA = Best corrected visual acuity

* BCVA measured using the Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity chart at a starting distance of 4 meters.

** All estimates are adjusted estimates based on a mixed-effect model with repeated measures. SUSVIMO arm - intravitreal ranibizumab arm. 95% is a rounding of 95.03% CI; The type 1 error was adjusted for interim sensitivity monitoring.

*** Equivalence margins were ± 4.5 letters.

Figure 29 Adjusted Mean change from Baseline in Best Corrected Visual Acuity in study eye through Week 48 in the Archway (GR40548) study*, **



* Prior to study treatment, a median of 4 doses of anti-VEGF intravitreal agents were administered in the study eye of patients in the SUSVIMO and intravitreal ranibizumab arms.

** Decrease in BCVA at Week 4 during post-operative recovery period.

Q24W = every 24 weeks; Q4W = every 4 weeks

Consistent results were observed across patient subgroup analyses for mean change from baseline in BCVA score (age, gender, number of prior anti-VEGF intravitreal injections, and baseline BCVA score).

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

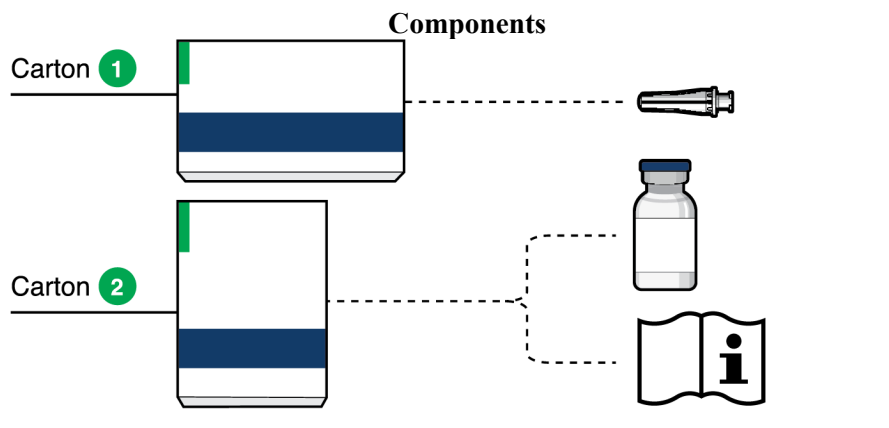
Each SUSVIMO initial fill needle kit (NDC 50242-078-55) contains:

- One SUSVIMO 100 mg/mL single-dose glass vial
- One SUSVIMO initial fill needle (34-gauge needle with a 5 µm integrated filter) with a blue cap

Each SUSVIMO (ranibizumab injection) carton (NDC 50242-078-12) contains one SUSVIMO (ranibizumab injection) 100 mg/mL that is clear to slightly opalescent, colorless to pale brown solution in a single-dose glass vial.

Each SUSVIMO refill needle carton contains a SUSVIMO refill needle (34-gauge vented needle with a 5 µm integrated filter) with a clear cap.

Device and Materials Description



- 1 SUSVIMO™**
Refill needle in
sterile blister
containing
- One refill needle

- 2 SUSVIMO™ (ranibizumab injection)**
100 mg/mL
containing
- One SUSVIMO™ (ranibizumab injection) vial
- One Prescribing Information

Figure 30

SUSVIMO implant

- SUSVIMO implant (Figure 31) is capable of holding 0.02 mL of drug, and is secured within the sclera, by the extrascleral flange that remains visible through the conjunctiva following insertion.
- The septum is a self-sealing interface through which ranibizumab is administered to fill the implant.

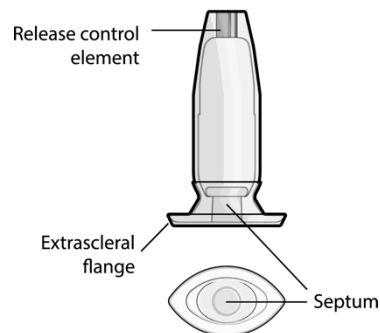


Figure 31

SUSVIMO (ranibizumab injection) 100 mg/mL vial

- SUSVIMO (ranibizumab injection) (Figure 32) is used to fill the implant with ranibizumab prior to insertion or during subsequent refill-exchange in an office-based setting.



Figure 32

SUSVIMO refill needle

- SUSVIMO refill needle (Figure 33) consists of a 34 G vented needle assembly, silicone soft stop, and a 5 µm integrated filter within the needle hub. It is designed to simultaneously exchange the contents of the implant reservoir with replacement ranibizumab in an office-based setting. As replacement ranibizumab is administered into the implant through the stainless-steel cannula, fluid remaining in the implant flows through openings in the vented needle and is collected in the fluid collection reservoir.

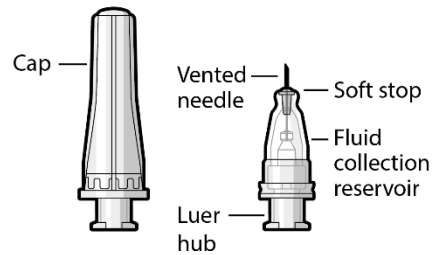


Figure 33

- SUSVIMO refill needle is distinguished by its clear cap.

Materials List

Materials that are required and supplied to perform the procedure are:

- SUSVIMO refill needle, 34 G, with clear cap
- SUSVIMO (ranibizumab injection) 100 mg/mL

Additional materials required to perform the procedure but are not provided are:

- One sterile 1 mL Luer Lock syringe (**not included**)
- One sterile 5-micron filter needle (19-gauge x 1½ inch) (**not included**)
- Anesthetic ophthalmic solutions
- Ophthalmic broad-spectrum microbicide solution
- Cotton tips and gauze
- Sterile powder free gloves
- Face masks
- Lid speculum
- Magnification such as visor or loupes
- Task lighting
- Indirect ophthalmoscope and lens
- Sterile drape (*optional for refill-exchange procedure*)

16.2 Storage

Store SUSVIMO initial fill needle kit at 2°C to 8°C (36°F to 46°F). **Do not** freeze. Protect from light. **Do not** shake. The SUSVIMO initial fill needle has been sterilized with electron beam processing.

Store SUSVIMO (ranibizumab injection) 100 mg/ mL vial at 2°C to 8°C (36°F to 46°F). **Do not** freeze. Protect from light. **Do not** shake. Prior to use, the unopened vial may be kept at 9°C to 30°C (48°F to 86°F) for up to 24 hours provided it is protected from light.

Store the SUSVIMO implant and insertion tool assembly, refill needle and explant tool at room temperature 15°C to 25°C (59°F to 77°F). The SUSVIMO implant and insertion tool assembly has been sterilized with ethylene oxide gas. The SUSVIMO refill needle and explant tool have been sterilized with electron beam processing.

16.3 Handling

SUSVIMO components are supplied sterile and are for single-use only. Do not reprocess, re-sterilize, or reuse SUSVIMO components. Do not use if the sterility has been compromised or the contents have been dropped, damaged or tampered with. Do not use past the expiration date printed on the label. Do not open sealed tray until time of use. Avoid contact between sharp surgical instruments and the SUSVIMO implant as the material of the septum and silicone encasing is soft and susceptible to damage.

Important Device Handling Information

- Use caution when performing ophthalmic procedures that may cause deflection of the implant and subsequent injury. For example, B-scan ophthalmic ultrasound, scleral depression, or gonioscopy.

Ocular Implant Initial Fill Procedure

- Minimize air bubbles within the implant reservoir as they may cause slower drug release. If an air bubble is present, it must be no larger than 1/3 of the widest diameter of the implant. If excess air is observed after initial fill, **do not** use the implant.

Ocular Implant Insertion Procedure

- Perpendicular entry of the implant is important to avoid contact between the implant and intraocular structures such as the lens, as contact between the implant and the intraocular structures may cause adverse reactions such as traumatic cataract.
- Avoid excessive force on the globe by first ensuring that the tip of the implant has passed through the sclero-pars plana incision before slowly pushing the implant into place.

Ocular Implant Removal Procedure

- **Do not** grasp the implant by the short axis of the implant flange. Remove the implant in a gentle manner. Perpendicular exit of the implant is important to avoid contact between the implant and intraocular structures such as the lens.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Advise patients on the following after the implant insertion procedure:

Positioning:

- Keep head above shoulder level for the rest of the day.
- Sleep with head on 3 or more pillows during the day and the night after surgery.

How to care for the treated eye after the procedure:

- Do not remove the eye shield until they are instructed to do so by their healthcare

provider. At bedtime, continue to wear the eye shield for at least 7 nights following the implant surgery.

- Administer all post-operative eye medications as directed by their healthcare provider.
- Do not push on the eye, rub the eye, or touch the area of the eye where the implant is located (underneath the eyelid in the upper and outer part of the eye) for 30 days following the implant insertion.
- Do not participate in strenuous activities until 1-month after the implant insertion or after discussion with their healthcare provider.

Magnetic Resonance (MR) Conditional information:

- The SUSVIMO implant is MR conditional. Inform their healthcare provider that they have SUSVIMO implanted in their eye and show their healthcare provider the SUSVIMO implant card should they require Magnetic resonance imaging (MRI).

Advise patients on the following after the Refill-Exchange procedure:

- Refrain from pushing on the treated eye, rubbing the eye, or touching the eye in the area of the implant (located underneath the eyelid in the upper and outer part of your eye) for 7 days following the refill-exchange procedure.
- Administer eye drops as directed by their healthcare provider.

Advise patients on the following after the implant removal procedure (if it is deemed medically necessary):

- Keep your head above shoulder level for the rest of the day.
- Sleep with your head on 3 or more pillows if lying down during the day and night after the implant removal.
- Wear an eye shield for at least 7 nights following the implant removal.
- Do not participate in strenuous activities until 14 days following the implant removal.
- Administer all post-operative anti-inflammatory and antimicrobial drops, as directed by your healthcare provider.

Advise patients on the following throughout SUSVIMO treatment:

- Do not drive or use machinery until the eye shield can be removed and visual function has recovered sufficiently [*see Adverse Reactions (6.1)*].
- The SUSVIMO implant and/or implant related procedures have been associated with conjunctival reactions (bleb, erosion, retraction), vitreous hemorrhage, endophthalmitis, rhegmatogenous retinal detachment, the dislocation of the implant, septum dislodgement, and a temporary decrease in vision.
- While the implant is in the eye, avoid rubbing the eye or touching the area as much as possible. However, if necessary to do so, make sure hands are cleaned prior to touching the eye.
- Seek immediate care from an ophthalmologist if there are sudden changes in their vision (an increase in moving spots, the appearance of “spider webs”, flashing lights, or a loss in vision), increasing eye pain, progressive vision loss, sensitivity to light, redness in the

white of the eye, a sudden sensation that something is in their eye, or eye discharge or watering [see *Warnings and Precautions (5)*].

SUSVIMO™ [ranibizumab injection]

Manufactured by:

Genentech, Inc.

A Member of the Roche Group

1 DNA Way

South San Francisco, CA 94080-4990

U.S. License No.: 1048

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MEDICATION GUIDE
SUSVIMO™ (suss-VIH-moh)
(ranibizumab injection)

for intravitreal use via SUSVIMO ocular implant

What is the most important information I should know about SUSVIMO?

SUSVIMO (ranibizumab injection) is delivered into the eye using the SUSVIMO implant. The SUSVIMO implant and the procedures to insert, fill, refill and remove the eye (ocular) implant can cause serious side effects including:

- **an eye infection (endophthalmitis).** Endophthalmitis is an infection of the eyeball that can cause permanent damage to your eye including blindness. **Call your healthcare provider right away if you have increasing eye pain, vision loss, sensitivity to light, or redness in the white of the eye.** Endophthalmitis requires urgent (same day) medical or surgical treatment.
- **a missing layer on top of the white part of the eye (conjunctival erosion).** Conjunctival erosion is an area that becomes missing (defect) in the layer (conjunctiva) that covers the white part of the eye which may result in exposure of the implant. **Call your healthcare provider right away if you have a sudden feeling that something is in your eye, if you have eye discharge, or watering of the eye.** Conjunctival erosion may require surgical treatment.
- **an opening of the layer that covers the white part of the eye (conjunctival retraction).** Conjunctival retraction is an opening or gaping in the layer (conjunctiva) that covers the white part of the eye which may cause the implant to be exposed. **Call your healthcare provider right away if you have a sudden feeling that something is in your eye, if you have eye discharge, or watering of the eye.** Conjunctival retraction may require surgical treatment.

See **“What are the possible side effects of SUSVIMO?”** for other serious side effects that may happen while in treatment with SUSVIMO.

To help prevent or keep these side effects from becoming more serious follow all post-procedure instructions your healthcare provider gives you. See “How will I receive SUSVIMO?”.

What is SUSVIMO?

SUSVIMO (ranibizumab injection) is a prescription medicine used to treat adults with Neovascular (wet) Age-related Macular Degeneration (AMD) who have responded to at least two injections of a Vascular Endothelial Growth Factor (VEGF) inhibitor in the gel-like part of the eye (intravitreal).

It is not known if SUSVIMO is safe and effective in children.

Do not receive SUSVIMO if you:

- have an infection in or around your eye.
- have active swelling around your eye that may include pain and redness.
- are allergic to ranibizumab or any of the ingredients in SUSVIMO. See the end of this Medication Guide for a complete list of ingredients in SUSVIMO.

Talk to your healthcare provider before receiving this SUSVIMO if you have any of these conditions.

Before receiving SUSVIMO, tell your healthcare provider about all of your medical conditions, including if you:

- are currently taking or have recently taken medicines that lower the chance of blood clots forming in the body such as warfarin, low or regular doses of aspirin, or nonsteroidal anti-inflammatory drugs (NSAID).
- are pregnant or plan to become pregnant. It is not known if SUSVIMO will harm your unborn baby. You should use birth control during your treatment with SUSVIMO and for 12 months after your last dose of SUSVIMO.
- are breastfeeding or plan to breastfeed. It is not known if SUSVIMO passes into your breast milk. Talk to your healthcare provider about the best way to feed your baby if you receive SUSVIMO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive SUSVIMO?

- SUSVIMO is implanted through the white part of the eye (sclera) by your healthcare provider.
- Your healthcare provider will refill your implant device every 6 months (about every 24 weeks).
- If you miss a scheduled refill, call your healthcare provider as soon as possible to reschedule your refill. Your next refill should be given 6 months after your last refill.

Your healthcare provider will give you instructions to follow after the implant insertion, the refill procedure, and the implant

removal. The instructions may include:

After the Implant Insertion:

- **Positioning of your head**
 - Keep your head above shoulder level for the rest of the day.
 - Sleep with your head on 3 or more pillows during the day and night after your implant insertion.
- **How to care for your eye**
 - **Do not** remove the eye shield from your eye until you are told to by your healthcare provider. At bedtime, continue to wear an eye shield for **at least 7 nights** following the implant insertion.
 - Take all post-operative eye medicines as your healthcare provider tells you to.
 - **Do not** push on the eye, rub the eye, or touch the area of the eye where the implant is located (underneath the eyelid in the upper and outer part of your eye) for **30 days** following the implant insertion.
 - **Do not** participate in strenuous activities until 1 month after the implant insertion or after talking to your healthcare provider.
- **Magnetic Resonance Imaging (MRI) Implant Card**
 - Get your implant card from your healthcare provider after receiving the implant and keep the card in a safe place for future reference. The implant card contains important information about your SUSVIMO implant.
 - Show your current and future healthcare providers your implant card. This is important if you need to have an MRI. You may only receive an MRI under very specific conditions if you have the SUSVIMO implant. Your healthcare provider will review the information on the implant card and will let you know if you should receive an MRI.

After the Refill Procedure:

- **Do not** push on the eye, rub the eye, or touch the area of the eye where the implant is located (underneath the eyelid in the upper and outer part of your eye) for **7 days** following the refill procedure.
- Take eye drops exactly as your healthcare provider tells you to take them.

After the Implant Removal:

- Keep your head above shoulder level for the rest of the day.
- Sleep with your head on 3 or more pillows if lying down during the day and night after implant removal.
- Wear an eye shield for **at least 7 nights** following the implant removal.
- Do not participate in strenuous activities until **14 days** following the implant removal.
- Give all post-operative drops, as told by your healthcare provider.

These are not all the instructions you may receive from your healthcare provider. Following all post-procedure instructions may help prevent serious side effects or keep side effects from becoming more serious. See **“What is the most important information I should know about SUSVIMO?”**.

What should I avoid while receiving SUSVIMO?

- **Do not** drive or use machinery until the eye shield can be removed and you can see.
- **Avoid** rubbing your eye or touching the area of your eye where the implant is located as much as possible while the implant is in place. If you have to rub or touch your eye, wash your hands first.

What are the possible side effects of SUSVIMO?

See **“What is the most important information I should know about SUSVIMO?”** on the first page.

In addition to those side effects listed on page one, the SUSVIMO implant and the procedures to insert, fill, refill and remove the eye (ocular) implant can cause other serious side effects including:

- **Tear and separation of layers of the retina (Rhegmatogenous retinal detachment).** Rhegmatogenous retinal detachment is a tear and separation of one of the layers of the retina in the back of the eye that senses light. Call your healthcare provider or go to the emergency room right away if you see flashing lights, see a curtain or veil covering part of your vision, have a change in your vision, or a loss of vision. Rhegmatogenous retinal detachment requires surgical treatment.
- **Implant movement (Implant dislocation):** Tell your healthcare provider right away if you notice that the implant has moved out of place. This movement may require surgical treatment to correct.
- **Implant damage:** Damage to the implant that prevents continued treatment (refills) with SUSVIMO. If the implant is not able to be properly refilled, your wet AMD may be inadequately treated and your physician may remove the implant and/or change your treatment.
- **Bleeding (Vitreous hemorrhage):** Vitreous hemorrhage is bleeding within the gel-like substance (vitreous) inside of

your eye. Call your healthcare provider right away if you have an increase in moving spots or what looks like spider webs in your vision as you may need an additional eye surgery.

- **Bump on top of the white layer of the eye (Conjunctival bleb):** Conjunctival bleb is a small bulge in the layer (conjunctiva) that covers the white part of the eye where the implant is inserted. This may be due to leakage of fluid from the inside of the eye. Call your healthcare provider right away if you have a sudden feeling that something is in your eye (foreign body sensation), see a bulge over the white part of your eye, if you have eye discharge, or watering in the eye. You may need medical or surgical treatment.
- **Temporary decrease in vision after the SUSVIMO procedure.**

The most common side effects of SUSVIMO include:

- blood on the white of the eye
- eye pain
- redness in the white of the eye
- sensitivity to light

These are not all the possible side effects of SUSVIMO.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

You may also report side effects to Genentech at 1-888-835-2555.

General information about the safe and effective use of SUSVIMO.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your pharmacist or healthcare provider for information about SUSVIMO that is written for health professionals.

What are the ingredients in SUSVIMO (ranibizumab injection)?

Active ingredient: ranibizumab

Inactive ingredients: histidine HCl, polysorbate 20, sucrose.

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