

AUSTRALIAN PRODUCT INFORMATION

SUSVIMO® (ranibizumab) for use with the Contivue ocular implant

▼ This medicinal product is subject to additional monitoring in Australia. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse events at <https://www.tga.gov.au/reporting-problems>.

WARNING: ENDOPHTHALMITIS

The Contivue 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 Contivue implant experienced at least one episode of endophthalmitis (see Sections 4.3 Contraindications and 4.4 Special warnings and precautions for use).

1. NAME OF THE MEDICINE

Ranibizumab

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial of 0.395 mL contains 39.5 mg of ranibizumab at a concentration of 100 mg/mL. This provides a usable amount to deliver a single dose of 0.1 mL solution required to fill the implant with approximately 0.02 mL (2 mg) of ranibizumab solution. The implant is designed to contain approximately 0.02 mL (2 mg) of ranibizumab solution when filled.

For the full list of excipients, see section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

Solution for injection for intravitreal use with the Contivue ocular implant.

Clear to slightly opalescent, colourless to slightly brownish liquid.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Susvimo is indicated for the treatment of adult patients with neovascular (wet) age-related macular degeneration (AMD) who have previously responded to at least two intravitreal injections of vascular endothelial growth factor (VEGF) inhibitors.

4.2 DOSE AND METHOD OF ADMINISTRATION

Dosage

Susvimo is intended for continuous delivery to the vitreous via the Contivue implant only. Do not administer Susvimo by any other route. Do not administer Susvimo as a bolus intravitreal injection. Do not substitute Susvimo with other ranibizumab products.

The initial fill and implant procedure and implant removal procedure must be performed under aseptic conditions by an ophthalmologist experienced in vitreoretinal surgery and trained in Contivue implant procedures. The implant refill-exchange procedure should be

performed under aseptic conditions by an ophthalmologist trained in the Susvimo refill-exchange procedure.

Read and refer to the manufacturer's Initial Fill and Implant Procedure, Refill-exchange Procedure, and Implant Removal Procedure instructions for use prior to initially filling, implanting, refilling or removing the Contivue implant.

Patient Selection

Patients should have responded to intravitreal anti-VEGF treatment prior to treatment with Susvimo.

Recommended Dosage

Susvimo has been specially developed for use with the Contivue implant.

The recommended dose of Susvimo is 2 mg (0.02 mL of 39.5 mg/0.395 mL) continuously delivered via the Contivue implant with refill-exchange procedures administered every 24 weeks (approximately 6 months).

Supplemental dosing with intravitreal ranibizumab injection

Supplemental treatment with 0.5 mg (10 mg/mL) intravitreal ranibizumab injection may be administered in the affected eye while the Contivue implant is in place and if clinically necessary (see section 5.1).

Refer to the full product information for 0.5 mg (10 mg/mL) intravitreal ranibizumab injection.

Duration of Treatment

Susvimo is intended for continuous treatment via the Contivue implant.

Delayed or Missed Doses (refill-exchange)

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

Dose (refill-exchange) Interruptions

For dose (refill-exchange) interruptions related to adverse events see Table 1. Following a refill-exchange interruption, perform refill-exchange procedure after resolution of the adverse event.

Table 1 Dose (refill-exchange) interruptions for Adverse Events

Adverse Event	Modification
Intraocular inflammation $\geq 2+$ cells or flare	Withhold dose (refill-exchange)
Sight threatening adverse events (e.g. retinal detachment, vitreous haemorrhage, 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 (see section 4.4)	Withhold dose (refill-exchange) Consider implant removal. Refer to manufacturer's <u>Implant Removal Procedure</u> instructions for use.
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Implant Removal

Implant removal can be performed at the physician's discretion should the benefit of removal outweigh the risk of the procedure. Refer to the manufacturer's Implant Removal Procedure Instructions for Use.

Special populations

Paediatric Use

The safety and efficacy of Susvimo in children and adolescents (<18 years) have not been established.

Geriatric Use

No dose adjustment of Susvimo is required in patients ≥ 65 years of age (see section 5.2).

Renal Impairment

No dose adjustment is required in patients with renal impairment (see section 5.2).

Hepatic Impairment

The safety and efficacy of Susvimo have not been established in patients with hepatic impairment. However, as systemic exposure is negligible, no dose adjustment is considered necessary in this population (see section 5.2).

Method of Administration

Single-dose vial for intravitreal use with the Contivue implant only. Susvimo is for single use in one patient only.

Susvimo should be inspected visually for particulate matter and discoloration prior to administration (see section 6.6).

The Contivue implant is initially filled with Susvimo prior to implant insertion (refer to Initial Fill and Implant Procedure Instructions for Use) and is refilled with Susvimo via an administration through the implant septum which is covered by the conjunctiva and Tenon's capsule (refer to the Refill-Exchange Procedure Instructions for Use). The appropriate needle should be used for the initial fill and implant procedure (initial fill needle) and the refill-exchange procedure (refill needle). The initial fill and implant insertion, and refill-exchange procedures should be performed with adequate anaesthesia under aseptic conditions to minimise the risk of intraocular infection as per standard of care.

4.3 CONTRAINDICATIONS

Susvimo is contraindicated in patients with a known hypersensitivity to ranibizumab or any of the excipients.

Susvimo is contraindicated in patients with active or suspected ocular or periocular infections.

Susvimo is contraindicated in patients with active intraocular inflammation.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Implant and Implant-related procedure adverse reactions

The implant and/or implant-related procedures have been associated with vitreous haemorrhage, conjunctival bleb/bleb leak, conjunctival erosion, conjunctival retraction, endophthalmitis, retinal detachment, device (implant) dislocation, septum dislodgement and post-surgical intraocular inflammation. Patients should be instructed to report signs or symptoms, if any, 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 carefully following the implant insertion and refill-exchange procedures to permit early medical or surgical intervention as necessary.

Strict adherence to the manufacturer's instructions for use for the Initial Fill and Implant Procedure, Refill-Exchange Procedure, and the Implant Removal Procedure is required to minimise procedure-related risks.

Vitreous Haemorrhage

Vitreous haemorrhages may result in temporary vision loss. Vitrectomy may be needed in the case of a non-clearing vitreous haemorrhage (see section 4.2).

Patients on antithrombotic medication (e.g. oral anticoagulants, aspirin, nonsteroidal anti-inflammatory drugs) may be at increased risk of vitreous haemorrhage. Antithrombotic medications are recommended to be temporarily interrupted prior to the implant insertion procedure.

Strict adherence to the manufacturer's instructions for use (e.g. appropriate pars plana laser ablation, scleral cauterisation) is required to minimise risks of vitreous haemorrhage.

Conjunctival Bleb/Bleb Leak

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 additional surgical and/or medical management to avoid further complications, especially if the implant septum is no longer identifiable due to the conjunctival bleb.

Strict adherence to the manufacturer's instructions for use (e.g. appropriate scleral incision length, appropriate incorporation of conjunctiva and Tenon's capsule in peritomy closure, appropriate seating of the refill needle during the Refill-Exchange Procedure) is required to minimise risks of conjunctival blebs.

Conjunctival Erosion

A conjunctival erosion is a full thickness degradation or breakdown of the conjunctiva in the area of the implant flange. Conjunctival erosions could be associated with an increased risk of endophthalmitis, especially if the implant becomes exposed.

Surgical intervention (e.g. conjunctival/Tenon's capsule repair) should be performed in case of conjunctival erosion with or without exposure of the implant flange.

Strict adherence to the manufacturer's instructions for use (e.g. appropriate incorporation of conjunctiva and Tenon's capsule in peritomy closure, appropriate placement of conjunctival sutures to avoid contact with the implant edge) is required to minimise risks of conjunctival

erosion.

Conjunctival Retraction

A conjunctival retraction is a recession or opening of the limbal and/or radial peritomy. Conjunctival retractions could be associated with an increased risk of endophthalmitis, especially if the implant becomes exposed. Surgical intervention (e.g. conjunctival/Tenon's capsule repair) should be performed in case of conjunctival retraction with or without exposure of the implant flange.

Strict adherence to the manufacturer's instructions for use (e.g. including appropriate suturing of the conjunctiva and Tenon's capsule to the limbus) is required to minimise risks of conjunctival retraction.

Endophthalmitis

Endophthalmitis requires prompt treatment as per standard of care to reduce the risk of vision loss and to maximise recovery. The Susvimo dose (refill-exchange) should be delayed until resolution of endophthalmitis (see sections 4.2 and 4.8).

Patients should not have an active or suspected ocular or periocular infection or severe systemic infection prior to any Susvimo procedure. Proper aseptic technique should always be used when administering Susvimo.

Strict adherence to the manufacturer's instructions for use (e.g. appropriate sterile controls during implant insertion or refill-exchange procedures) is required to minimise risks of endophthalmitis.

Retinal Detachment

Retinal detachment may result in vision loss if not promptly treated with an intervention (e.g. pneumatic retinopexy, vitrectomy, or laser photocoagulation). Delay the Susvimo dose (refill-exchange) until the retinal detachment has been treated (see section 4.2).

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

Strict adherence to the manufacturer's instructions for use (e.g. appropriate management of vitreous prolapse after pars plana incision) is required to minimise risks of retinal detachment.

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 the Contivue implant (see sections 4.8 and 5.1).

Device (implant) Dislocation

The device (implant) may dislocate or subluxate into the vitreous cavity, or extend outside the vitreous cavity into or beyond the subconjunctival space. Device dislocation requires urgent surgical intervention if it is associated with a positive Seidel test, retinal detachment, appositional choroidal detachment, conjunctival opening with vitreous leak and implant

expulsion (open globe), or the dislocated device is resting on or near the macula to prevent vision loss.

Strict adherence to the manufacturer's instructions for use (e.g. appropriate scleral incision length, appropriate targeting of the pars plana during laser ablation) is required to minimise risks of implant dislocation.

Septum Dislodgement

In clinical trials, a type of implant damage where the septum has dislodged into the body of the implant 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 following septum dislodgement and consider implant removal should the benefit of the removal procedure outweigh the risk (see section 4.2). The benefits and risks of retaining, removing, or removing and replacing an implant with a dislodged septum are not well characterised.

Strict adherence to the manufacturer's instructions for use [e.g. appropriate handling and insertion of the refill needle into the septum (avoid twisting and/or rotation)] is required to minimise the risk of septum dislodgement.

Post procedural intraocular inflammation

There is a risk of intraocular inflammation following Susvimo procedures (e.g. implantation, refill-exchange), consistent with the risk inherent to intraocular procedures. The majority of events experienced during clinical trials occurred within the first week following Susvimo procedures and resolved within one month. Use peri-operative anti-inflammatory agents as per standard of care and at the ophthalmologist's discretion. Patients should be instructed to report any signs or symptoms of intraocular inflammation to their ophthalmologist.

Bilateral treatment

In clinical trials, the majority of patients with neovascular (wet) age related macular degeneration (nAMD) in the fellow eye received treatment with an anti VEGF intravitreal injection and a limited number of patients received Susvimo in the fellow eye. Due to the small number of patients with bilateral treatment with Susvimo to date, the safety and efficacy of Susvimo administered in both eyes have not been established.

Other

In the event a patient required a magnetic resonance imaging (MRI) scans, the procedure should be performed under specific conditions as the implant contains titanium. It is, therefore, important that patients are informed and are given an implant card which should be kept with them at all times and shown to healthcare professionals if they require an MRI scan. The device manufacturer's instructions for use for the initial fill and implant procedure provide the scan conditions to safely perform an MRI scan for a patient with this implanted device.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

No drug-drug interaction studies have been performed.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

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 may pose a risk to reproductive capacity.

Women of childbearing potential

Women of childbearing potential should use effective contraception while receiving Susvimo and for 12 months following the last dose (refill-exchange) of Susvimo.

Use in pregnancy

Category D

No clinical studies of Susvimo in pregnant women have been performed.

No reproductive and developmental toxicity studies have been conducted with ranibizumab delivered via the implant.

An embryo-fetal developmental toxicity study with intravitreal ranibizumab was performed on pregnant cynomolgus monkeys. Pregnant animals received intravitreal ranibizumab injections 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 after treatment of a single eye with Susvimo. No skeletal abnormalities were seen at the lower dose of 0.125 mg/eye, a dose which resulted in trough concentrations equivalent to single eye treatment with Susvimo in humans. No effect on the weight or structure of the placenta, maternal toxicity, or embryotoxicity was observed.

The systemic exposure to Susvimo is low after administration via the Contivue implant, but due to its mechanism of action, Susvimo must be regarded as potentially teratogenic and embryo-fetotoxic. The absence of ranibizumab-mediated effects on the embryo-fetal development in the monkey study at doses equivalent to single eye treatment with Susvimo in humans is plausibly related to the expected inability of the Fab fragment to cross the placenta. Nevertheless, ranibizumab was detected in a fetus coincident with high maternal ranibizumab and anti-ranibizumab antibody serum levels, possibly because the anti-ranibizumab antibody acted as a (Fc region containing) carrier protein for ranibizumab, thereby decreasing its maternal serum clearance and enabling its placental transfer.

Therefore, Susvimo is not recommended during pregnancy unless the expected benefit outweighs the potential risk to the fetus. The Contivue implant may be flushed with saline using a refill needle should the patient become pregnant.

The safe use of Susvimo during labour and delivery has not been established.

Use in lactation

It is not known whether Susvimo is excreted in human breast milk. No studies have been conducted to assess the impact of Susvimo on milk production or its presence in breast milk.

Susvimo is not recommended during breast-feeding.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Susvimo, Contivue, implant related-procedures and associated examinations have a moderate influence on the ability to drive and use machines. Patients may experience temporarily reduced vision after implant-related procedures and the associated eye examination. Patients should not drive or use machines until the eye shield can be removed and visual function has recovered (see section 4.8).

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The ARCHWAY trial had 248 patients with nAMD who underwent the SUSVIMO initial fill and implant insertion, refill, and implant removal (if necessary) procedures up to Week 40. The safety data from ARCHWAY are summarised in Table 2.

**Table 2 Ocular Adverse Events in Study Eye through Week 40, ARCHWAY
Safety Population ($\geq 5\%$ in Either Arm)**

MedDRA System organ class	Susvimo (%) N = 248			Intravitreal ranibizumab (%) N = 167		
	Onset within 37 days	Onset after 37 days	Overall	Onset within 37 days	Onset after 37 days	Overall
Eye disorders						
Conjunctival haemorrhage	71.0	4.8	71.4	3.0	3.0	6.0
Conjunctival hyperaemia	25.0	2.8	26.6	0	1.8	1.8
Iritis	19.4	1.2	20.2	0	0	0
Eye pain	10.1	0.4	10.1	1.8	3.0	4.8
Vitreous floaters	4.4	4.4	8.9	0.6	1.8	2.4
Vitreous detachment	1.6	3.6	5.2	0	4.8	4.8
Foreign body sensation in eyes	7.3	0.4	7.3	0	1.2	1.2
Punctate keratitis	4.0	2.4	6.0	0.6	1.8	2.4
Vitreous haemorrhage	4.8	0.4	5.2	0.6	1.8	2.4
Conjunctival bleb	4.0	2.4	6.5"	0	0	0
Hypotony of eye	5.6	0.4	6.0	0	0	0

Summary of the safety profile

The safety profile of Susvimo has been evaluated in 577 nAMD patients.

This safety profile includes adverse reactions related to Susvimo, Contivue, the Initial Fill and Implant, Refill-Exchange, and Implant Removal Procedures. In this pooled patient population, the:

- most frequent ($\geq 10\%$) adverse reactions overall were conjunctival haemorrhage (72.1%), conjunctival hyperaemia (25.6%), iritis (24.8%), eye pain (20.6%), cataract (18.5%), conjunctival bleb/filtering bleb leak (14.7%), vitreous floaters (13.2%) and headache (11.6%)
 - most frequent ($\geq 10\%$) adverse reactions during the postoperative period (within 37 days of initial implantation) were conjunctival haemorrhage (65.9%), conjunctival hyperaemia (21.5%), iritis (20.8%), and eye pain (12.0%)
- most frequent ($\geq 1\%$) serious adverse reactions overall were septum dislodgement (9.5%), conjunctival erosion (4.5%), endophthalmitis (2.6%), conjunctival bleb/bleb leak (1.9%), device dislocation (1.9%), conjunctival retraction (1.7%), and retinal detachment (1.0%)
- adverse reactions ($\geq 0.5\%$) that resulted in implant removal were septum dislodgement (4.9%), conjunctival erosion (1.6%), conjunctival retraction (1.0%), endophthalmitis (1.0%), and device dislocation (0.9%)

Tabulated summary of adverse reactions from clinical trials

Adverse reactions from clinical trials (Table 3) are listed by MedDRA system organ class. The corresponding frequency category for each adverse drug reaction is based on the following convention: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$), very rare ($< 1/10,000$).

Table 3 Summary of adverse reactions occurring in patients treated with Susvimo in clinical trials

MedDRA System organ class	Susvimo All Grades (%) N = 577	Frequency Category
Eye Disorders		
Conjunctival haemorrhage	72.1	Very common
Conjunctival hyperaemia	25.6	Very common
Iritis ¹	24.8	Very common
Eye pain	20.6	Very common
Cataract ²	18.5	Very common
Conjunctival bleb/ filtering bleb leak ³	14.7	Very common
Vitreous floaters	13.2	Very common
Retinal haemorrhage	9.2	Common
Foreign body sensation in eyes	8.8	Common

Conjunctival erosion	7.8	Common
Eye irritation	7.6	Common
Vitreous haemorrhage	7.5	Common
Hypotony of eye	6.9	Common
Vitreous detachment	6.9	Common
Vision blurred	6.6	Common
Conjunctival oedema	6.4	Common
Blepharitis	6.2	Common
Corneal abrasion ⁴	5.7	Common
Eyelid ptosis	5.2	Common
Corneal oedema	4.3	Common
Eye pruritus	4.3	Common
Visual acuity reduced	4.0	Common
Conjunctival retraction	3.5	Common
Intraocular pressure decreased	3.5	Common
Scleral thinning	2.9	Common
Endophthalmitis ⁵	2.8	Common
Corneal disorder ⁶	2.6	Common
Lacrimation increased	2.6	Common
Ocular discomfort	2.6	Common
Photophobia	2.6	Common
Conjunctivitis	2.4	Common
Eyelid oedema	2.4	Common
Device dislocation	2.4	Common
Procedural pain	2.3	Common
Vitritis	2.1	Common
Choroidal detachment	1.7	Common
Ecchymosis	1.7	Common
Hyphema	1.7	Common
Iridocyclitis	1.7	Common
Conjunctival thinning	1.4	Common
Eye discharge	1.4	Common
Iris adhesions	1.4	Common
Retinal detachment ⁷	1.4	Common
Conjunctival disorder	0.9	Uncommon
Device material opacification ⁸	0.9	Uncommon
Scleral hyperaemia	0.9	Uncommon
Suture related complication	0.9	Uncommon
Post procedural discomfort	0.7	Uncommon
Retinal tear	0.7	Uncommon
Implant site fibrosis	0.5	Uncommon
Tenon's capsule thickening	0.5	Uncommon

Administration site discomfort ⁹	0.3	Uncommon
Foreign body in eye	0.3	Uncommon
Post procedural swelling	0.2	Uncommon
Injury, Poisoning and Procedural Complications		
Headache	11.6	Very common
Nausea	7.3	Common
Vomiting	2.4	Common
Product Issues		
Septum Dislodgement ¹⁰	9.9	Common

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

² Cataract: includes cataract, cataract nuclear, cataract cortical, cataract subcapsular and cataract traumatic

³ Conjunctival bleb/filtering bleb leak: includes conjunctival bleb, conjunctival filtering bleb leak, conjunctival cyst and implant site cyst

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

⁵ In clinical studies the management of endophthalmitis included a flush of implant contents with 100 µL of vancomycin (1.0 mg), with or without previous flush with saline, in addition to standard of care.

⁶ Corneal disorder: includes corneal disorder and corneal endothelial disorder

⁷ Retinal detachment: includes retinal detachment, rhegmatogenous retinal detachment and tractional retinal detachment

⁸ Device material opacification: reported as opacities of unknown aetiology within implant

⁹ Administration site discomfort: reported as refill site irritation - discomfort

¹⁰ Septum dislodgement: a type of implant damage where the septum dislodges into the body of the implant. The incidence of septum dislodgement was calculated from implanted patients across Susvimo clinical trials

Description of selected adverse reactions

Vitreous haemorrhage

In the Susvimo arm, 7.5% (43/577) of patients reported vitreous haemorrhage in the study eye. Based on a functional grading system, the majority of patients (31/43) reported Grade 1 [<15 letter best corrected visual acuity (BCVA) loss from previous visit] and Grade 2 (16-30 letter BCVA loss from previous visit) events. Overall, most patients reported vitreous haemorrhage events that resolved spontaneously (34/43 patients).

During the post-operative period, 4.5% (26/577) of patients reported vitreous haemorrhage events. In this period, 14/26 patients reported Grade 1 vitreous haemorrhage events and 5/26 patients reported Grade 2 vitreous haemorrhage events.

Conjunctival bleb/Conjunctival filtering bleb leak

In the Susvimo arm, 14.7% (85/577) of patients reported conjunctival bleb/conjunctival filtering bleb leak in the study eye and 5.0% (29/577) of patients reported these events in the post-operative period. The majority of patients reported conjunctival bleb/conjunctival filtering bleb leak events that were mild (71/85 patients) or moderate (10/85 patients).

Conjunctival erosion

In the Susvimo arm, 7.8% (45/577) of patients reported conjunctival erosion in the study eye and 0.3% (2/577) of patients reported these events during the post-operative period. The majority of patients reported conjunctival erosion events that were mild (14/45 patients) or

moderate (21/45 patients). 7/45 patients discontinued Susvimo treatment due to conjunctival erosion.

Conjunctival retraction

In the Susvimo arm, 3.5% (20/577) of patients in the Susvimo arm reported conjunctival retraction in the study eye and 0.7% (4/577) of patients reported these events during the post-operative period. The majority of patients reported conjunctival retraction events that were mild (9/20 patients) or moderate (9/20 patients). 6/20 patients had the implant removed as a result of conjunctival retraction.

Endophthalmitis

In the Susvimo arm, 2.8% (16/577) of patients reported endophthalmitis in the study eye. These patients reported endophthalmitis events that were moderate (4/16 patients) or severe (12/16 patients). Of these patients, 8/16 reported preceding or concurrent conjunctival retraction or conjunctival erosion events and 6/16 patients had the implant removed as a result of endophthalmitis. 8/16 patients discontinued Susvimo treatment due to endophthalmitis.

Retinal detachment

In the Susvimo arm, 1.4% (8/577) of patients reported retinal detachment in the study eye and 0.3% (2/577) of patients reported these events in the post-operative period. All patients experienced retinal detachment events that were severe.

Device (implant) dislocation

In the Susvimo arm, 2.4% (14/577) of patients reported device dislocation events in the study eye. The majority of device dislocation events reported were moderate or severe. Of these patients, 5/14 had the implant removed and 8/14 discontinued treatment with Susvimo.

Postmarketing Experience

Not applicable

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product.

Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Based on the Contivue implant fill volume of 0.02 mL, the maximum amount of Susvimo that can be initially filled and subsequently refilled is approximately 2 mg. Doses of ranibizumab as high as 2 mg have been administered via intravitreal injection. The adverse drug reactions observed at the 2 mg intravitreal dose were consistent with those reported for the 0.5 mg intravitreal ranibizumab dose in clinical trials.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Ophthalmologicals, antineovascularisation agents. ATC code: S01LA04

Mechanism of Action

Ranibizumab is a humanised recombinant monoclonal antibody fragment targeted against human vascular endothelial growth factor A (VEGF-A). It binds with high affinity to all biologically active VEGF-A isoforms (e.g. VEGF110, VEGF121 and VEGF165), thereby preventing binding of VEGF-A to its receptors VEGFR-1 and VEGFR-2.

Binding of VEGF-A to its receptors leads to endothelial cell proliferation and neovascularisation, as well as vascular leakage, which contribute to the progression of the neovascular form of age-related macular degeneration.

Pharmacodynamic effect

Leakage of blood and fluid from choroidal neovascularisation (CNV) may cause retinal thickening or oedema and/or intraretinal/subretinal haemorrhage, resulting in vision loss.

In Archway, the related anatomical parameters of centre point thickness [measured from internal limiting membrane (ILM) to retinal pigment epithelium] and central subfield thickness (measured from ILM to Bruch's membrane) were assessed.

At week 36, a similar adjusted mean change in centre point thickness (CPT) was observed between Susvimo arm and intravitreal ranibizumab arm patients (5.4 microns vs 2.6 microns, respectively). This corresponded to a difference in adjusted means of 2.8 microns (95.03% CI: - 6.2, 11.9) between arms.

At week 36, a similar adjusted mean change in central subfield thickness (CST) was observed between Susvimo arm and intravitreal ranibizumab arm patients (10.3 vs 4.4 microns, respectively). This corresponded to a difference in adjusted means of 5.9 microns (95.03% CI: -2.9, 14.7) between arms.

Clinical trials

The clinical efficacy and safety of Susvimo were assessed in a randomised, visual assessor-masked, open-label active treatment-controlled study [Archway (GR40548)] in patients with nAMD. 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 any type of macular CNV related to 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. At the screening visit, patients received an additional intravitreal injection of 0.5 mg ranibizumab if they received only 3 doses of anti-VEGF intravitreal agents within the last 6 months and/or if the last treatment received prior to screening was not 0.5 mg ranibizumab. Each patient had a demonstrated response to anti-VEGF intravitreal agents defined as: overall decrease in nAMD disease activity detected on spectral-domain optical coherence tomography (SD-OCT) and stable or improved vision. Patients were randomised in a 3:2 ratio to receive continuous delivery of Susvimo via the implant every 24 weeks or 0.5 mg intravitreal ranibizumab injections every 4 weeks. For patients randomised to the Susvimo arm, supplemental treatment with intravitreal injections

of 0.5 mg ranibizumab was available at Weeks 16, 20, 40, 44, 64, 68, 88, and 92 if one of the following criteria was met and due to nAMD disease activity: a loss of 15 letters from the best recorded Best Corrected Visual Acuity (BCVA) value on study, an increase of 150 microns from the lowest CST value on study, or a loss of 10 letters from the highest BCVA value associated with an increase of 100 microns from the lowest CST value.

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. The mean change in visual acuity in the study eye from diagnosis of nAMD to baseline was 11.3 Early Treatment Diabetic Retinopathy Study (ETDRS) letters. Of the patients assessed for supplemental treatment in the Susvimo arm, 98.4%, 94.6%, 94.8% and 94.7% did not receive supplemental treatment in the first, second, third and fourth treatment intervals, respectively.

The primary efficacy endpoint of change from baseline in BCVA score averaged over Week 36 and Week 40 demonstrated Susvimo to be non-inferior and equivalent to intravitreal ranibizumab injections administered every 4 weeks. Detailed efficacy results are shown in Table 4 and Figure 1.

Table 4 Visual acuity outcomes in the Archway (GR40548) study

Outcome Measure*	Susvimo 100mg/mL n=248	Intravitreal ranibizumab 0.5 mg (10mg/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)***
Adjusted Mean change from baseline in BCVA score averaged over Weeks 44 and 48	0.0	0.2	-0.2 (-1.8, 1.3)****
Adjusted Mean change from baseline in BCVA score averaged over weeks 88 and 92	-1.1	-0.5	-0.6 (-2.5, 1.3)****
Adjusted Proportion of patients with BCVA score of 69 letters (20/40 approximate Snellen equivalent) or better averaged over Weeks 36 and 40	80.7%	82.1%	-1.4% (-7.4%, 4.5%)
Adjusted Proportion of patients who lose < 10 letters in BCVA score from baseline averaged over Weeks 36 and 40	95.1%	95.1%	0.0% (-4.2%, 4.3%)

BCVA = Best corrected visual acuity

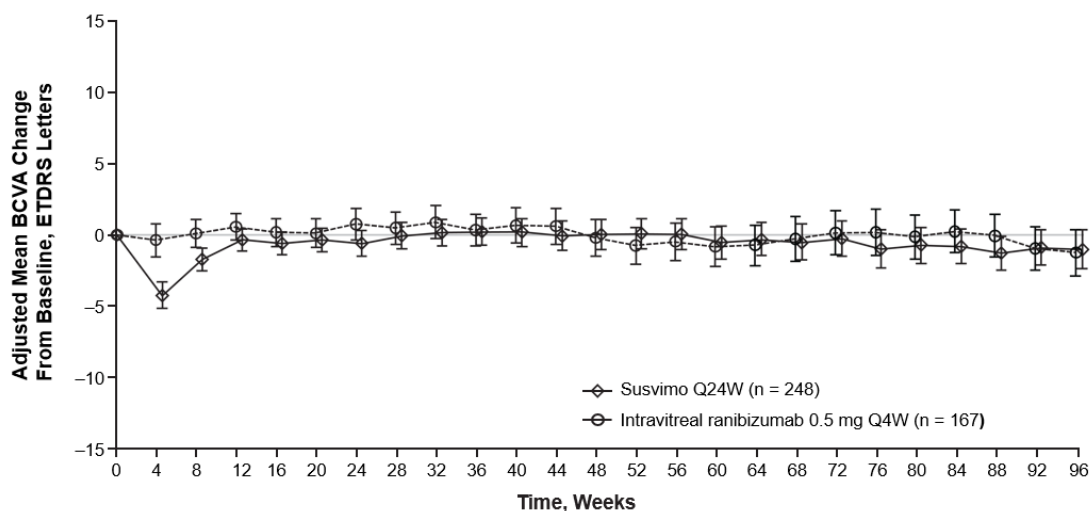
* BCVA measured by ETDRS letters score

**All estimates are adjusted estimates based on a mixed-effect model with repeated measures or Cochran-Mantel-Haenszel (CMH) weighted estimates. Susvimo arm – intravitreal ranibizumab arm. 95% is a rounding of 95.03% confidence interval (CI); The type 1 error was adjusted for interim safety monitoring.

*** Non-inferiority margin was -4.5 letters. Equivalence margins were ± 4.5 letters. Non-inferiority was also met at -3.9 letter margin as a key secondary endpoint.

**** Non-inferiority was met at -3.9 letter margin as key secondary end point.

Figure 1 Adjusted mean change from baseline in BCVA in study eye through week 96 in the Archway (GR40548) study*



Q24W = every 24 weeks; Q4W = every 4 weeks

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

Consistent results were observed across patient subgroup analyses for mean change from baseline in BCVA score averaged over weeks 36 and 40 (age, gender, number of prior anti-VEGF intravitreal injections, and baseline BCVA score) and centre point thickness at week 36 (age and gender).

Patient Preference Questionnaire

At Week 40, 218 of 234 patients (93.2%) reported preferring continuous delivery of Susvimo over intravitreal ranibizumab injections. The most common reasons cited were fewer treatments (175/218) and less discomfort (164/218). At week 40, 3 of 234 patients (1.3%) preferred intravitreal ranibizumab injections over Susvimo. 13 of 234 patients (5.6%) had no preference for either route of administration. 14 out of 248 patients (5.6%) did not complete the Patient Preference Questionnaire.

Immunogenicity

As with all therapeutic proteins, there is the potential for an immune response to Susvimo. The detection of an immune response is highly dependent on the sensitivity and 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 incidence of antibodies to Susvimo with the incidence of antibodies to other products may be misleading.

Prior to treatment with Susvimo, 2.1% (5 of 243) of patients with nAMD tested positive for anti-ranibizumab antibodies. After treatment with Susvimo, 13.4% (33 of 247) of patients tested positive for anti-ranibizumab antibodies.

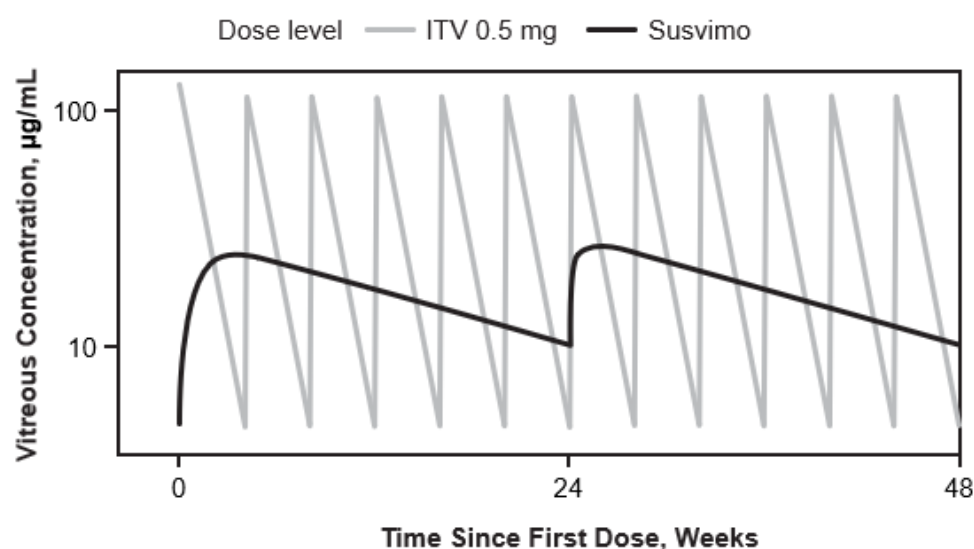
No clinically meaningful differences in the pharmacokinetics, efficacy, or safety were observed in patients testing positive for anti-ranibizumab antibodies.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Susvimo delivered via the Contivue implant provides continuous delivery of ranibizumab into the vitreous, with the release of ranibizumab decreasing over time as the concentration in the implant decreases. Vitreous concentrations with Susvimo are predicted to be below the maximum and above the minimum concentrations experienced with monthly 0.5 mg intravitreal ranibizumab (see Figure 2).

Figure 2 Predicted vitreous ranibizumab concentration with Susvimo with refill-exchanges every 24 weeks compared to monthly 0.5 mg intravitreal ranibizumab injections



ITV = intravitreal ranibizumab

Distribution

Ranibizumab is distributed from the vitreous to the aqueous humor and serum. The ranibizumab concentrations in aqueous humor decrease with a half-life of approximately 15 weeks. The ranibizumab serum concentrations decrease with a half-life of approximately 29 weeks. Ranibizumab did not accumulate in serum when administered with refill-exchange procedures every 24 weeks.

Following implant insertion, 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-exchange procedures with Susvimo in patients with nAMD, maximum serum concentrations of ranibizumab were below the ranibizumab concentration necessary to inhibit the biological activity of VEGF by 50%.

Metabolism

The metabolism of Susvimo has not been directly studied. Susvimo is a monoclonal antibody fragment. Antibodies are cleared principally by catabolism.

Elimination

Vitreous and serum pharmacokinetics following treatment with Susvimo exhibit rate-limited elimination, driven by the release of ranibizumab from the Contivue implant (see section 5.2, Absorption).

Special populations

Renal impairment

No formal study has been conducted to examine the pharmacokinetics of Susvimo in patients with renal impairment. In a population pharmacokinetic analysis of nAMD patients with Susvimo, 73% (266 of 364) had renal impairment (44% mild [CrCL 60 to < 90 mL/min], 27% moderate [CrCL 30 to < 60 mL/min] and 2% severe [CrCL < 30 mL/min]). Systemic clearance of ranibizumab was found to be 2-fold lower in a patient with creatinine clearance of 30 mL/min compared to a patient with creatinine clearance of 90 mL/min. Given that the serum concentrations of ranibizumab are low relative to the levels required to affect systemic VEGF, these differences are not clinically significant.

Hepatic impairment

No formal study has been conducted to examine the pharmacokinetics of Susvimo in patients with hepatic impairment.

Use in the Elderly

In population pharmacokinetic analysis of nAMD patients with Susvimo, patients ranged in age from 50 to 92 years old. Age did not have a significant effect on the pharmacokinetics of Susvimo.

Paediatric use

No studies have been conducted to investigate the pharmacokinetics of Susvimo in this population.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No studies have been performed to establish the mutagenic potential of Susvimo.

Carcinogenicity

No carcinogenicity studies have been performed to establish the carcinogenic potential of Susvimo.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Histidine hydrochloride

Polysorbate 20

Sucrose

Water for injections

6.2 INCOMPATIBILITIES

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 SHELF LIFE

36 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store at 2°C-8°C in the outer carton in order to protect from light.

Prior to use, the unopened vial may be kept below 30°C for up to 24 hours.

Do not freeze. Do not shake.

6.5 NATURE AND CONTENTS OF CONTAINER

One vial (type I glass with a fluoro-resin laminated stopper and an aluminium flip-off cap) containing 0.395 mL sterile solution

6.6 SPECIAL PRECAUTIONS FOR USE, HANDLING AND DISPOSAL

Read and refer to the appropriate manufacturer's Initial Fill and Implant Procedure, Refill-Exchange Procedure, and Implant Removal Procedure Instructions for Use prior to filling, implanting, refilling or removing the Contivue implant.

Strict aseptic procedures must be used during the preparation and handling of the Susvimo vial and when filling and refilling the Contivue implant. The implant initial fill and implant insertion and implant removal procedures must be performed in an operating room by an ophthalmologist experienced in vitreoretinal surgery and trained in the implant procedures. The implant refill-exchange procedure should be performed by an ophthalmologist trained in the implant refill-exchange procedures (see section 4.2).

Susvimo vials should be inspected visually for particulate matter and discolouration prior to administration. Susvimo is a clear to slightly opalescent, colourless to slightly brownish liquid. Do not use Susvimo if the medicine has particulate matter, cloudiness or discolouration.

The contents of the vial are supplied sterile and are for single use in one patient only. Do not reprocess, resterilise, or reuse any component. Do not use any component if it is damaged, broken, or the sterility has been compromised.

In Australia, any unused medicine or waste material should be disposed of by taking it to your local pharmacy.

6.7 PHYSIOCHEMICAL PROPERTIES

Chemical structure

Ranibizumab is a humanised monoclonal antibody fragment produced in E. coli expression vector by standard recombinant DNA technology.

It consists of one heavy chain VHIII (231 amino acid residues) and one light chainVL kI (214 amino acid residues) subgroup sequences.

The approximate molecular weight of intact ranibizumab is 48 kDa.

CAS number:

347396-82-1

7. MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine

8. SPONSOR

Roche Products Pty Limited

ABN 70 000 132 865

Level 8, 30 – 34 Hickson Road

Sydney NSW 2000

AUSTRALIA

Medical enquiries: 1800 233 950

9. DATE OF FIRST APPROVAL

24 September 2026

10. DATE OF REVISION OF THE TEXT

24 September 2026

Summary of Changes Table

Section Changed	Summary of new information