

**ANNEX I**  
**SUMMARY OF PRODUCT CHARACTERISTICS**

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

## **1. NAME OF THE MEDICINAL PRODUCT**

Beovu 120 mg/ml solution for injection in pre-filled syringe  
Beovu 120 mg/ml solution for injection

## **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

One ml solution for injection contains 120 mg of brolocizumab\*.

\* Brolocizumab is a humanised monoclonal single-chain Fv (scFv) antibody fragment produced in *Escherichia coli* cells by recombinant DNA technology.

### Beovu 120 mg/ml solution for injection in pre-filled syringe

Each pre-filled syringe contains 19.8 mg brolocizumab in 0.165 ml solution. This provides a usable amount to deliver a single dose of 0.05 ml solution containing 6 mg of brolocizumab.

### Beovu 120 mg/ml solution for injection

Each vial contains 27.6 mg brolocizumab in 0.23 ml solution. This provides a usable amount to deliver a single dose of 0.05 ml solution containing 6 mg of brolocizumab.

For the full list of excipients, see section 6.1.

## **3. PHARMACEUTICAL FORM**

Solution for injection (injection).

Clear to slightly opalescent, colourless to slightly brownish-yellow aqueous solution.

## **4. CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

Beovu is indicated in adults for the treatment of neovascular (wet) age-related macular degeneration (AMD).

### **4.2 Posology and method of administration**

Beovu must be administered by a qualified ophthalmologist experienced in intravitreal injections.

#### Posology

The recommended dose is 6 mg brolocizumab (0.05 ml solution) administered by intravitreal injection every 4 weeks (monthly) for the first 3 doses. Thereafter, the physician may individualise treatment intervals based on disease activity as assessed by visual acuity and/or anatomical parameters. A disease activity assessment is suggested 16 weeks (4 months) after treatment start. In patients without disease activity, treatment every 12 weeks (3 months) should be considered. In patients with disease

activity, treatment every 8 weeks (2 months) should be considered. The physician may further individualise treatment intervals based on disease activity.

If visual and anatomical outcomes indicate that the patient is not benefiting from continued treatment, Beovu should be discontinued.

#### Special populations

##### *Elderly*

No dosage adjustment is required in patients aged 65 years or above (see section 5.2).

##### *Renal impairment*

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

##### *Hepatic impairment*

Brolucizumab has not been studied in patients with hepatic impairment. No dosage adjustment is required in patients with hepatic impairment (see section 5.2).

##### *Paediatric population*

The safety and efficacy of brolucizumab in children and adolescents below 18 years of age have not been established. No data are available.

#### Method of administration

Beovu is for intravitreal use only.

The solution for injection should be inspected visually prior to administration (see section 6.6).

The intravitreal injection procedure should be carried out under aseptic conditions, which includes the use of surgical hand disinfection, sterile gloves, a sterile drape and a sterile eyelid speculum (or equivalent). Sterile paracentesis equipment should be available as a precautionary measure. The patient's medical history for hypersensitivity reactions should be carefully evaluated prior to performing the intravitreal procedure (see section 4.3). Adequate anaesthesia and a broad-spectrum topical microbicide to disinfect the periocular skin, eyelid and ocular surface should be administered prior to the injection.

The injection needle should be inserted 3.5 to 4.0 mm posterior to the limbus into the vitreous cavity, avoiding the horizontal meridian and aiming towards the centre of the globe. The injection volume of 0.05 ml is then delivered slowly; a different scleral site should be used for subsequent injections.

Immediately following the intravitreal injection, patients should be monitored for elevation in intraocular pressure. Appropriate monitoring may consist of a check for perfusion of the optic nerve head or tonometry. If required, sterile equipment for paracentesis should be available.

Following intravitreal injection patients should be instructed to report any symptoms suggestive of endophthalmitis (e.g. eye pain, redness of the eye, photophobia, blurring of vision) without delay.

#### Pre-filled syringe

The pre-filled syringe is for single use only. Each pre-filled syringe should only be used for the treatment of a single eye.

Since the volume contained in the pre-filled syringe (0.165 ml) is greater than the recommended dose (0.05 ml), a portion of the volume contained in the pre-filled syringe must be discarded prior to administration.

Injecting the entire volume of the pre-filled syringe could result in overdose. To expel the air bubble along with excess medicinal product, the plunger should be slowly depressed until the edge below the dome of the rubber stopper is aligned with the 0.05 ml dose mark (equivalent to 50 µl, i.e. 6 mg brolocizumab).

#### Vial

The vial is for single use only. Each vial should only be used for the treatment of a single eye.

Since the volume contained in the vial (0.23 ml) is greater than the recommended dose (0.05 ml), a portion of the volume contained in the vial must be discarded prior to administration.

Injecting the entire volume of the vial could result in overdose. To expel the air bubble along with excess medicinal product, the air should be carefully expelled from the syringe and the dose adjusted to the 0.05 ml mark (equivalent to 50 µl, i.e. 6 mg brolocizumab).

For instructions on preparation of the medicinal product before administration, see section 6.6.

### **4.3 Contraindications**

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Patients with active or suspected ocular or periocular infections.

Patients with active intraocular inflammation.

### **4.4 Special warnings and precautions for use**

#### Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

#### Intravitreal injection-related reactions

Intravitreal injections, including those with Beovu, have been associated with endophthalmitis, intraocular inflammation, traumatic cataract and retinal detachment (see section 4.8). Retinal artery occlusion has been reported with the use of Beovu (see section 4.8). Proper aseptic injection techniques must always be used when administering Beovu. Patients should be instructed to report any symptoms suggestive of the above-mentioned events without delay.

#### Intraocular pressure increases

Transient increases in intraocular pressure have been seen within 30 minutes of intravitreal injection with vascular endothelial growth factor (VEGF) inhibitors, including brolocizumab (see section 4.8). Special precaution is needed in patients with poorly controlled glaucoma (do not inject Beovu while the intraocular pressure is  $\geq 30$  mmHg). Both intraocular pressure and perfusion of the optic nerve head must be monitored and managed appropriately.

#### Bilateral treatment

The safety and efficacy of brolocizumab administered in both eyes concurrently have not been studied.

### Immunogenicity

As this is a therapeutic protein, there is a potential for immunogenicity with brolocizumab (see section 4.8). Patients should be instructed to inform their physician if they develop symptoms such as eye pain or increased discomfort, worsening eye redness, blurred or decreased vision, an increased number of small particles in their vision, or increased sensitivity to light (see section 4.8).

### Concomitant use of other anti-VEGF

There are no data available on the concomitant use of Beovu with other anti-VEGF medicinal products in the same eye. Brolocizumab should not be administered concurrently with other anti-VEGF medicinal products (systemic or ocular).

### Withholding treatment

In intravitreal anti-VEGF treatments, the dose should be withheld and treatment should not be resumed earlier than the next scheduled treatment in the event of:

- a decrease in best-corrected visual acuity (BCVA) of  $\geq 30$  letters compared with the last assessment of visual acuity;
- a retinal break;
- a subretinal haemorrhage involving the centre of the fovea, or, if the size of the haemorrhage is  $\geq 50\%$  of the total lesion area;
- performed or planned intraocular surgery within the previous or next 28 days.

### Retinal pigment epithelial tear

Risk factors associated with the development of a retinal pigment epithelial tear after anti-VEGF therapy for wet AMD include a large and/or high pigment epithelial retinal detachment. When initiating brolocizumab therapy, caution should be used in patients with these risk factors for retinal pigment epithelial tears.

### Rhegmatogenous retinal detachment or macular holes

Treatment should be discontinued in subjects with rhegmatogenous retinal detachment or stage 3 or 4 macular holes.

### Systemic effects following intravitreal use

Systemic adverse events, including non-ocular haemorrhages and arterial thromboembolic events, have been reported following intravitreal injection of VEGF inhibitors and there is a theoretical risk that these may relate to VEGF inhibition. There are limited data on safety in the treatment of patients with AMD with a history of stroke, transient ischaemic attacks or myocardial infarction within the last 3 months. Caution should be exercised when treating such patients.

### Sodium content

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially “sodium-free”.

## **4.5 Interaction with other medicinal products and other forms of interaction**

No interaction studies have been performed.

## **4.6 Fertility, pregnancy and lactation**

### Women of childbearing potential

Women of childbearing potential should use effective contraception during treatment with brolocizumab and for at least one month after the last dose when stopping treatment with brolocizumab.

### Pregnancy

There are no or limited amount of data from the use of brolocizumab in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). Although the systemic exposure after ocular administration is very low, brolocizumab should not be used during pregnancy unless the potential benefit outweighs the potential risk to the foetus.

### Breast-feeding

It is unknown whether brolocizumab is excreted in human milk. A risk to the breast-fed newborn/infant cannot be excluded. Brolocizumab is not recommended during breast-feeding and breast-feeding should not be started for at least one month after the last dose when stopping treatment with brolocizumab. A decision must be made whether to discontinue breast-feeding or to abstain from brolocizumab therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

### Fertility

No reproductive or fertility studies have been conducted. VEGF inhibition has been shown to affect follicular development, corpus luteum function and fertility. Based on the mechanism of action of VEGF inhibitors, there is a potential risk for female reproduction, and to embryofetal development.

## **4.7 Effects on ability to drive and use machines**

Beovu has a minor influence on the ability to drive and use machines due to possible temporary visual disturbances following the intravitreal injection and the associated eye examination. Patients should not drive or use machines until visual function has recovered sufficiently.

## **4.8 Undesirable effects**

### Summary of the safety profile

The most frequently reported adverse reactions were reduced visual acuity (7.3%), cataract (7.0%), conjunctival haemorrhage (6.3%) and vitreous floaters (5.1%).

The most serious adverse reactions were blindness (0.8%), endophthalmitis (0.7%), retinal artery occlusion (0.8%) and retinal detachment (0.7%).

### Tabulated list of adverse reactions

Adverse reactions (Table 1) are listed according to the MedDRA system organ class. Within each system organ class, the adverse reactions are ranked by frequency, with the most frequent reactions first. Frequency categories for each adverse reaction are 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 ( $< 1/10,000$ ). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

**Table 1** Frequencies of adverse reactions in clinical studies

<b>MedDRA System organ class</b>	<b>Frequency category</b>
<b>Immune system disorders</b>	
Hypersensitivity (including urticaria, rash, pruritus, erythema)	Common
<b>Eye disorders</b>	
Visual acuity reduced	Common
Retinal haemorrhage	Common
Uveitis	Common
Iritis	Common
Vitreous detachment	Common
Retinal tear	Common
Cataract	Common
Conjunctival haemorrhage	Common
Vitreous floaters	Common
Eye pain	Common
Intraocular pressure increase	Common
Conjunctivitis	Common
Retinal pigment epithelial tear	Common
Vision blurred	Common
Corneal abrasion	Common
Punctate keratitis	Common
Blindness	Uncommon
Endophthalmitis	Uncommon
Retinal artery occlusion	Uncommon
Retinal detachment	Uncommon
Conjunctival hyperaemia	Uncommon
Lacrimation increased	Uncommon
Abnormal sensation in eye	Uncommon
Detachment of retinal pigment epithelium	Uncommon
Vitritis	Uncommon
Anterior chamber inflammation	Uncommon
Iridocyclitis	Uncommon
Anterior chamber flare	Uncommon
Corneal oedema	Uncommon
Vitreous haemorrhage	Uncommon

Description of selected adverse reactionsImmunogenicity

There is a potential for an immune response in patients treated with Beovu. After dosing with Beovu for 88 weeks, treatment-emergent anti-brolucizumab antibodies were detected in 23–25% of patients. Among patients with treatment-emergent antibodies, a higher number of intraocular inflammation adverse reactions were observed. The clinical significance of anti-brolucizumab antibodies on safety is unclear at this time. Anti-brolucizumab antibodies were not associated with an impact on clinical efficacy.

Product-class-related adverse reactions

There is a theoretical risk of arterial thromboembolic events, including stroke and myocardial infarction, following intravitreal use of VEGF inhibitors. A low incidence rate of arterial thromboembolic events was observed in the brolucizumab clinical studies in patients with AMD. There were no major notable differences between the groups treated with brolucizumab and comparator.

## Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 via the national reporting system listed in [Appendix V](#).

### **4.9 Overdose**

Overdosing with greater than recommended injection volume may increase intraocular pressure. In the event of overdose, intraocular pressure should therefore be monitored and, if deemed necessary by the treating physician, appropriate treatment should be initiated.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Ophthalmologicals, antineovascularisation agents, ATC code: S01LA06

#### Mechanism of action

Brolucizumab is a humanised monoclonal single chain Fv (scFv) antibody fragment with a molecular weight of ~26 kDa.

Increased levels of signalling through the vascular endothelial growth factor A (VEGF-A) pathway are associated with pathological ocular angiogenesis and retinal oedema. Brolucizumab binds with high affinity to VEGF-A isoforms (e.g. VEGF<sub>110</sub>, VEGF<sub>121</sub>, and VEGF<sub>165</sub>), thereby preventing binding of VEGF-A to its receptors VEGFR-1 and VEGFR-2. By inhibiting VEGF-A binding, brolucizumab suppresses endothelial cell proliferation, thereby reducing pathological neovascularisation and decreasing vascular permeability.

#### Pharmacodynamic effects

Neovascular (wet) age-related macular degeneration (AMD) is characterised by pathological choroidal neovascularisation (CNV). Leakage of blood and fluid from CNV may cause retinal thickening or oedema and/or intraretinal/subretinal haemorrhage, resulting in loss of visual acuity.

In the HAWK and HARRIER studies, related anatomical parameters were part of the disease activity assessments guiding treatment decisions. Reductions in central subfield thickness (CST) and in presence of intraretinal/subretinal fluid (IRF/SRF) or sub-retinal pigment epithelium (sub-RPE) fluid were observed in patients treated with Beovu as early as 4 weeks after treatment initiation and up to week 48 and week 96.

At week 16, the reduction in CST was statistically significant on Beovu versus aflibercept in both studies (HAWK: -161 vs. -134 microns; HARRIER: -174 vs. -134 microns). This decrease from baseline in CST was also statistically significant at week 48 (HAWK: -173 vs. -144 microns; HARRIER: -194 vs. -144 microns), and maintained to the end of each study at week 96 (HAWK: -175 vs. -149 microns; HARRIER: -198 vs. -155 microns).

At week 16, the percentage difference in patients with IRF and/or SRF fluid was statistically significant on Beovu versus aflibercept in both studies (HAWK: 34% vs. 52%; HARRIER: 29% vs. 45%). This difference was also statistically significant at week 48 (HAWK: 31% vs. 45%; HARRIER: 26% vs. 44%), and maintained to the end of each study at week 96 (HAWK: 24% vs. 37%; HARRIER: 24% vs. 39%).



At week 16, the percentage difference in patients with sub-RPE fluid was statistically significant on Beovu versus aflibercept in both studies (HAWK: 19% vs. 27%; HARRIER: 16% vs. 24%). This difference was also statistically significant at week 48 (HAWK: 14% vs. 22%; HARRIER: 13% vs. 22%), and maintained to the end of each study at week 96 (HAWK: 11% vs. 15%; HARRIER: 17% vs. 22%).

In these studies, for patients treated with Beovu, reductions in CNV lesion size were observed as early as 12 weeks, and at weeks 48 and 96 after treatment initiation.

#### Clinical efficacy and safety

The efficacy and safety of Beovu were assessed in two randomised, multicentre, double-masked, active-controlled Phase III studies (HAWK and HARRIER) in patients with neovascular (wet) AMD. A total of 1,817 patients were treated in these studies for two years (1,088 on Beovu and 729 on comparator aflibercept). Patient ages ranged from 50 to 97 years, with a mean age of 76 years.

In both studies, after the first three monthly doses (weeks 0, 4 and 8), brolucizumab patients were treated every 12 weeks, with the option of adjusting to a dosing interval every 8 weeks based on disease activity. Disease activity was assessed by a physician during the first 12-week interval (at weeks 16 and 20) and at each subsequent scheduled 12-weekly treatment visit. Patients who showed disease activity (e.g. decreased visual acuity, increased CST and/or presence of IRF/SRF or sub-RPE fluid) at any of these visits were adjusted to an 8-weekly treatment interval. The comparator aflibercept was administered every 8 weeks after the first 3 monthly doses.

#### Results

The primary efficacy endpoint for the studies was the change from baseline in best corrected visual acuity (BCVA) to week 48, as measured by the early treatment diabetic retinopathy study (ETDRS) letter score, with the primary objective being to demonstrate non-inferiority of Beovu versus aflibercept. In both studies, Beovu (administered in an every 12 weeks or an every 8 weeks regimen) demonstrated non-inferior efficacy to aflibercept 2 mg (administered every 8 weeks). The visual acuity gains observed in the first year were maintained in the second year.

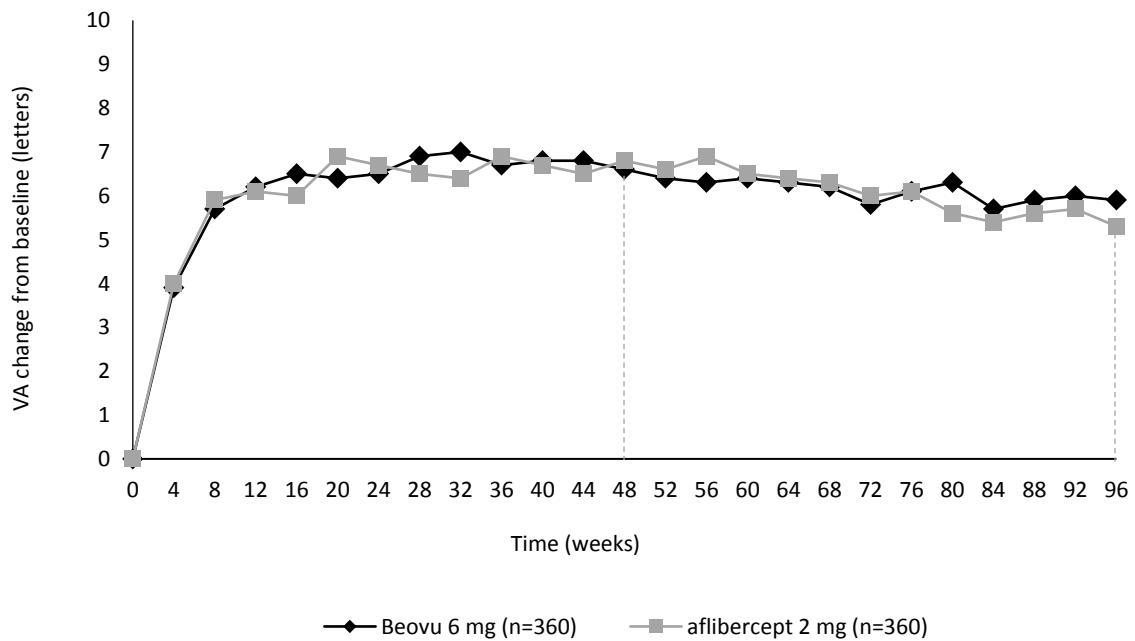
Detailed results of both studies are shown in Table 2 and in Figure 1 below.

**Table 2 Visual acuity outcomes at weeks 48 and 96 in Phase III - HAWK and HARRIER studies**

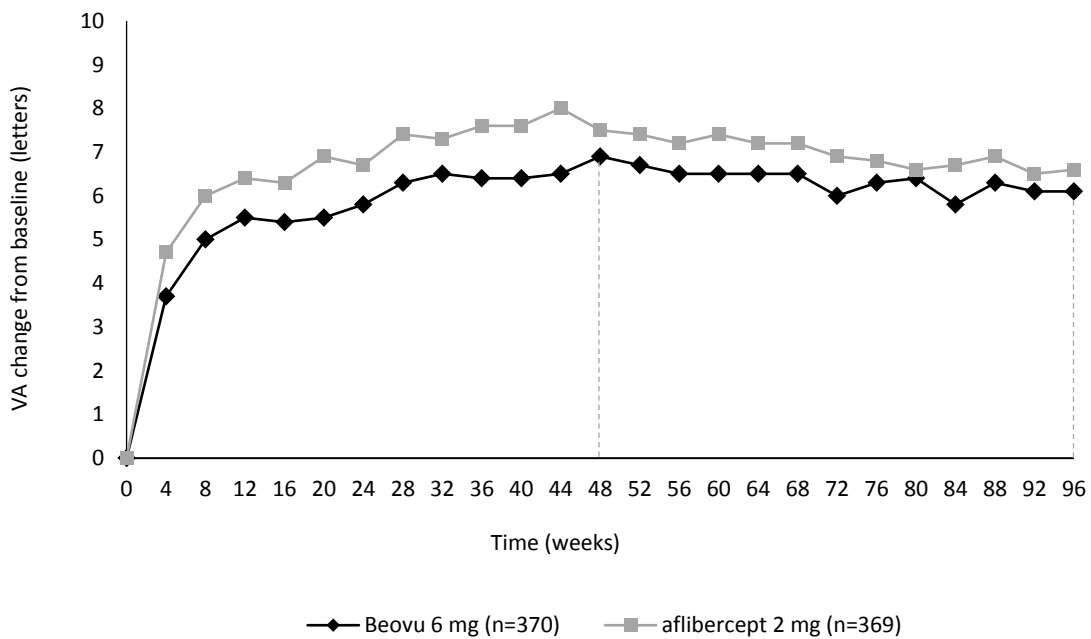
Efficacy outcome	Week	HAWK			HARRIER		
		Beovu 6 mg (n=360)	Aflibercept 2 mg (n=360)	Difference (95% CI) brolucizumab – aflibercept	Beovu 6 mg (n=370)	Aflibercept 2 mg (n=369)	Difference (95% CI) brolucizumab – aflibercept
Mean change from baseline in BCVA (measured by ETDRS letters score)	48	6.6 (SE=0.71)	6.8 (SE=0.71)	-0.2 (-2.1, 1.8) P<0.0001 <sup>a)</sup>	6.9 (SE=0.61)	7.6 (SE=0.61)	-0.7 (-2.4, 1.0) P<0.0001 <sup>a)</sup>
	36 – 48 <sup>b)</sup>	6.7 (SE=0.68)	6.7 (SE=0.68)	0.0 (-1.9, 1.9) P<0.0001 <sup>a)</sup>	6.5 (SE=0.58)	7.7 (SE=0.58)	-1.2 (-2.8, 0.4) P=0.0003 <sup>a)</sup>
	96	5.9 (SE=0.78)	5.3 (SE=0.78)	0.5 (-1.6, 2.7)	6.1 (SE=0.73)	6.6 (SE=0.73)	-0.4 (-2.5, 1.6)
% of patients who gained at least 15 letters of vision	48	33.6	25.4	8.2 (2.2, 15.0)	29.3	29.9	-0.6 (-7.1, 5.8)
	96	34.2	27.0	7.2 (1.4, 13.8)	29.1	31.5	-2.4 (-8.8, 4.1)
% of patients who lost visual acuity (%) (≥15 letters of BCVA loss)	48	6.4	5.5	0.9 (-2.7, 4.3)	3.8	4.8	-1.0 (-3.9, 2.2)
	96	8.1	7.4	0.7 (-3.6, 4.6)	7.1	7.5	-0.4 (-3.8, 3.3)
BCVA: best corrected visual acuity; missing data are imputed using last observation carried forward (LOCF) method ETDRS: early treatment diabetic retinopathy study <sup>a)</sup> P-value referring to the non-inferiority hypothesis with a non-inferiority margin of 4.0 letters. <sup>b)</sup> Key secondary endpoint, accounting for differences in timing of Beovu and aflibercept treatments.							

**Figure 1 Mean change in visual acuity from baseline to week 96 in HAWK and HARRIER studies**

**HAWK**



**HARRIER**



These visual acuity gains were achieved with 56% and 51% of patients treated with Beovu 6 mg on a 12-weekly dosing interval at week 48, and with 45% and 39% of patients at week 96 in HAWK and HARRIER, respectively. Among patients identified as eligible for the 12-weekly regimen during the first 12-week interval, 85% and 82% remained on the 12-weekly dosing interval up to week 48. Of patients on the 12-weekly interval at week 48, 82% and 75% remained on the 12-weekly dosing interval up to week 96.

Treatment effects in evaluable subgroups (e.g. age, gender, race, baseline visual acuity, baseline retinal thickness, lesion type, lesion size, fluid status) in each study were generally consistent with the results in the overall populations.

Disease activity was assessed by changes in visual acuity and/or anatomical parameters, including CST and/or presence of IRF/SRF or sub-RPE. Disease activity was assessed throughout the studies. Anatomical parameters of disease activity were decreased at week 48 and at week 96 for Beovu compared to aflibercept (see “Pharmacodynamic effects”).

The percentage difference in patients with disease activity at week 16 was statistically significant on Beovu versus aflibercept (24% vs 35% in HAWK,  $p=0.0013$ ; 23% vs 32% in HARRIER,  $p=0.0021$ ).

In both studies, Beovu demonstrated clinically meaningful increases from baseline in the pre-specified secondary efficacy endpoint of patient-reported outcomes, reported through the National Eye Institute Visual Function Questionnaire (NEI VFQ-25). The magnitude of these changes was similar to that seen in published studies, which corresponded to a 15-letter gain in BCVA. Patient-reported outcome benefits were maintained in the second year.

No clinically meaningful differences were found between Beovu and aflibercept in changes from baseline to week 48 in NEI VFQ-25 total score and subscales (general vision, ocular pain, near activities, distance activities, social functioning, mental health, role difficulties, dependency, driving, colour vision and peripheral vision).

#### Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Beovu in all subsets of the paediatric population in neovascular AMD (see section 4.2 for information on paediatric use).

## **5.2 Pharmacokinetic properties**

Beovu is administered directly into the vitreous to exert local effects in the eye.

#### Absorption and distribution

After intravitreal administration of 6 mg brolocizumab per eye to patients with nAMD, the geometric mean  $C_{max}$  of free brolocizumab in the plasma was 49.0 ng/ml (range: 8.97 to 548 ng/ml) and was attained in 1 day.

#### Biotransformation and elimination

Brolocizumab is a monoclonal antibody fragment and no metabolism studies have been conducted. As a single-chain antibody fragment, free brolocizumab is expected to undergo elimination through both target-mediated disposition via binding to free endogenous VEGF, passive renal elimination and metabolism via proteolysis.

After intravitreal injections, brolocizumab was eliminated with an apparent systemic half-life of 4.4 days. Concentrations were generally near or below the quantitation limit (<0.5 ng/ml) approximately 4 weeks after dosing in most patients. Brolocizumab did not accumulate in the serum when administered intravitreally every 4 weeks.

## Special populations

### Elderly

There were no relevant differences in systemic pharmacokinetics following intravitreal injection in a study with 22 patients aged 65 to 74 years, 18 patients aged 75 to 84 years and 3 patients aged  $\geq 85$  years.

### Renal impairment

The systemic pharmacokinetics of brolocizumab was evaluated in nAMD patients with normal renal function ( $\geq 90$  ml/min [n=21]), with mild (60 to  $< 90$  ml/min [n=22]) or moderate (30 to  $< 60$  ml/min [n=7]) renal impairment. While the mean systemic clearance values for patients with mild or moderate renal impairment were generally lower than patients with normal renal function, no significant impact of mild and moderate renal impairment on the overall systemic exposure to brolocizumab was observed. No patients with severe ( $< 30$  ml/min) renal impairment were studied.

### Hepatic impairment

Brolocizumab has not been studied in patients with hepatic impairment. Mild to severe hepatic impairment should have no impact on the overall systemic exposure to brolocizumab, because metabolism occurs via proteolysis and does not depend on hepatic function.

## **5.3 Preclinical safety data**

No studies have been conducted on the carcinogenic or mutagenic potential of brolocizumab.

No animal reproduction studies have been conducted.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Sodium citrate  
Sucrose  
Polysorbate 80  
Water for injections

### **6.2 Incompatibilities**

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

### **6.3 Shelf life**

Pre-filled syringe: 18 months  
Vial: 2 years

### **6.4 Special precautions for storage**

#### Pre-filled syringe

Store in a refrigerator (2°C - 8°C).

Do not freeze.

Keep the pre-filled syringe in its sealed blister and in the outer carton in order to protect from light. Prior to use, the unopened blister may be kept at room temperature (below 25°C) for up to 24 hours.

## Vial

Store in a refrigerator (2°C - 8°C).

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Prior to use, the unopened vial may be kept at room temperature (below 25°C) for up to 24 hours.

## **6.5 Nature and contents of container**

### Pre-filled syringe

0.165 ml sterile solution in a pre-filled syringe (type I glass) with a bromobutyl rubber plunger stopper and a syringe cap consisting of a white, tamper-evident rigid seal with a grey bromobutyl rubber tip cap including a Luer lock adapter. The pre-filled syringe has a plunger rod and a purple finger grip, and is packed in a sealed blister.

Pack size of 1 pre-filled syringe.

## Vial

0.230 ml sterile solution in a glass vial with a coated rubber stopper sealed with an aluminium cap with a purple plastic flip-off disk.

Pack size of 1 vial and 1 blunt filter needle (18G x 1½", 1.2 mm x 40 mm, 5 µm).

## **6.6 Special precautions for disposal and other handling**

### Pre-filled syringe

The pre-filled syringe contains more than the recommended dose of 6 mg. The extractable volume of the pre-filled syringe (0.165 ml) is not to be used in total. The excess volume should be expelled prior to injection. Injecting the entire volume of the pre-filled syringe could result in overdose. To expel the air bubble along with the excess medicinal product, slowly push the plunger until the edge below the dome of the rubber stopper is aligned with the black dosing line on the syringe (equivalent to 0.05 ml, i.e., 6 mg brolocizumab).

The solution should be inspected visually upon removal from the refrigerator and prior to administration. If particulates or cloudiness are visible, the pre-filled syringe must not be used and appropriate replacement procedures followed.

The pre-filled syringe is sterile and for single use only. Do not use if the packaging, or pre-filled syringe are damaged or expired. Detailed instructions for use are provided in the package leaflet.

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

## Vial

The vial contains more than the recommended dose of 6 mg. The extractable volume of the vial (0.23 ml) is not to be used in total. The excess volume should be expelled prior to injection. Injecting the entire volume of the vial could result in overdose. The injection dose must be set to the 0.05 ml dose mark, i.e. 6 mg brolocizumab.

The solution should be inspected visually upon removal from the refrigerator and prior to administration. If particulates or cloudiness are visible, the vial must not be used, and appropriate replacement procedures must be followed.

The content of the vial and the filter needle are sterile and for single use only. Do not use if the packaging, vial and/or filter needle are damaged or expired. Detailed instructions for use are provided in the package leaflet.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

**7. MARKETING AUTHORISATION HOLDER**

Novartis Europharm Limited  
Vista Building  
Elm Park, Merrion Road  
Dublin 4  
Ireland

**8. MARKETING AUTHORISATION NUMBER(S)**

EU/1/19/1417/001-002

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

**10. DATE OF REVISION OF THE TEXT**

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu>.

## **ANNEX II**

- A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**



**A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturer(s) of the biological active substance(s)

Lonza AG  
Lonzastrasse  
3930 Visp  
Switzerland

Novartis Pharma AG  
Lichtstrasse 35  
4056 Basel  
Switzerland

Sandoz GmbH  
Biochemiestrasse 10  
6250 Kundl  
Austria

AGC Biologics GmbH  
Czernyring 22  
69115 Heidelberg  
Germany

PHAST GmbH  
Kardinal-Wendel-Strasse 16  
66424 Homburg  
Germany

Name and address of the manufacturer(s) responsible for batch release

S.A. Alcon-Couvreur N.V.  
Rijksweg 14  
2870 Puurs  
Belgium

**B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

**C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**

• **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

## **D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Additional risk minimisation measures**

Prior to launch in each Member State the MAH shall agree the final educational material with the National Competent Authority.

The MAH shall ensure that, following discussions and agreements with the National Competent Authority in each Member State where Beovu is marketed, all ophthalmological clinics where Beovu is expected to be used are provided with a patient guide in written and audio format, including the following key elements:

- What is neovascular (wet) age-related macular degeneration
- What is Beovu, how does it work, how is it administered and what to expect from the treatment
- What are the steps following treatment with Beovu
- Description of the risks, including increased intraocular pressure, intraocular inflammation, retinal detachment & retinal tear and endophthalmitis, and their key signs and symptoms; signs and symptoms of immunogenicity
- Recommendations for monitoring and required examinations: Following intravitreal injection: measurement of increased intraocular pressure and perfusion of the optic nerve
- When and how to seek urgent attention from the health care provider

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**CARTON – PRE-FILLED SYRINGE**

**1. NAME OF THE MEDICINAL PRODUCT**

Beovu 120 mg/ml solution for injection in pre-filled syringe  
brolocizumab

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each pre-filled syringe of 0.165 ml solution contains 19.8 mg brolocizumab (120 mg/ml).

**3. LIST OF EXCIPIENTS**

Contains: sodium citrate, sucrose, polysorbate 80, water for injections.

**4. PHARMACEUTICAL FORM AND CONTENTS**

Solution for injection

1x 0.165 ml pre-filled syringe  
Delivers a single dose of 6 mg/0.05 ml.

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Read the package leaflet before use.  
Intravitreal use  
For single use only.  
After opening the sterile sealed blister, proceed under aseptic conditions.  
Set dose to 0.05 ml dose mark.  
Excess volume to be expelled prior to injection.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY**

**8. EXPIRY DATE**

EXP

**9. SPECIAL STORAGE CONDITIONS**

Store in a refrigerator.

Do not freeze.

Keep the pre-filled syringe in its sealed blister and in the outer carton in order to protect from light.

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Novartis Europharm Limited  
Vista Building  
Elm Park, Merrion Road  
Dublin 4  
Ireland

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/19/1417/001

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY**

**15. INSTRUCTIONS ON USE**

**16. INFORMATION IN BRAILLE**

Justification for not including Braille accepted.

**17. UNIQUE IDENTIFIER – 2D BARCODE**

2D barcode carrying the unique identifier included

**18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

PC  
SN  
NN

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**PEEL-OFF LABEL AFFIXED TO INNER LID OF CARTON – PRE-FILLED SYRINGE**

**1. NAME OF THE MEDICINAL PRODUCT**

Beovu

**2. EXPIRY DATE**

EXP

**3. BATCH NUMBER**

Lot

**MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS**

**BLISTER FOIL – PRE-FILLED SYRINGE**

**1. NAME OF THE MEDICINAL PRODUCT**

Beovu 120 mg/ml solution for injection in pre-filled syringe  
brolocizumab

**2. NAME OF THE MARKETING AUTHORISATION HOLDER**

Novartis Europharm Limited

**3. EXPIRY DATE**

EXP

**4. BATCH NUMBER**

Lot

**5. OTHER**

0.165 ml



**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**LABEL – PRE-FILLED SYRINGE**

**1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION**

Beovu 120 mg/ml injection  
brolocizumab  
Intravitreal use

**2. METHOD OF ADMINISTRATION**

**3. EXPIRY DATE**

EXP

**4. BATCH NUMBER**

Lot

**5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT**

19.8 mg/0.165 ml

**6. OTHER**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**CARTON – VIAL**

**1. NAME OF THE MEDICINAL PRODUCT**

Beovu 120 mg/ml solution for injection  
brolucizumab

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each vial of 0.23 ml solution contains 27.6 mg brolucizumab (120 mg/ml).

**3. LIST OF EXCIPIENTS**

Contains: sodium citrate, sucrose, polysorbate 80, water for injections.

**4. PHARMACEUTICAL FORM AND CONTENTS**

Solution for injection

1x 0.23 ml vial, 1 filter needle.  
Delivers a single dose of 6 mg/0.05 ml.

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Read the package leaflet before use.  
Intravitreal use  
For single use only.  
After opening the vial, proceed under aseptic conditions.  
Set dose to 0.05 ml.  
Excess volume to be expelled prior to injection.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY**

**8. EXPIRY DATE**

EXP

**9. SPECIAL STORAGE CONDITIONS**

Store in a refrigerator.  
Do not freeze.  
Keep the vial in the outer carton in order to protect from light.

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Novartis Europharm Limited  
Vista Building  
Elm Park, Merrion Road  
Dublin 4  
Ireland

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/19/1417/002

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY**

**15. INSTRUCTIONS ON USE**

**16. INFORMATION IN BRAILLE**

Justification for not including Braille accepted.

**17. UNIQUE IDENTIFIER – 2D BARCODE**

2D barcode carrying the unique identifier included

**18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

PC  
SN  
NN

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**LABEL - VIAL**

**1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION**

Beovu 120 mg/ml injection  
brolocizumab  
Intravitreal use

**2. METHOD OF ADMINISTRATION**

**3. EXPIRY DATE**

EXP

**4. BATCH NUMBER**

Lot

**5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT**

27.6 mg/0.23 ml

**6. OTHER**

**B. PACKAGE LEAFLET**

## Package leaflet: Information for the patient

### Beovu 120 mg/ml solution for injection in pre-filled syringe brolucizumab

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

**Read all of this leaflet carefully before you are given this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

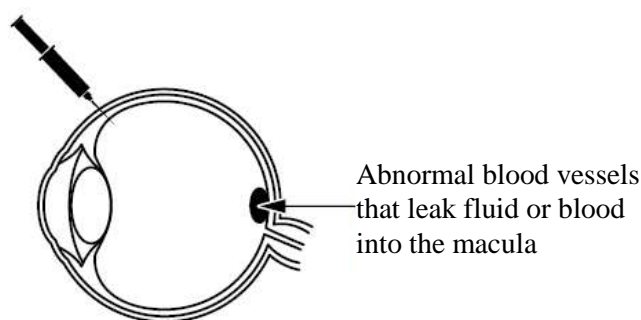
#### What is in this leaflet

1. What Beovu is and what it is used for
2. What you need to know before you are given Beovu
3. How Beovu is given
4. Possible side effects
5. How to store Beovu
6. Contents of the pack and other information

#### 1. What Beovu is and what it is used for

##### What Beovu is

Beovu contains the active substance brolucizumab, which belongs to a group of medicines called antineovascularisation agents. Beovu is injected into the eye by your doctor to treat an eye disorder called neovascular (wet) age-related macular degeneration (AMD).



##### What Beovu is used for

Beovu is used to treat neovascular wet AMD in adults, which occurs when abnormal blood vessels form and grow underneath the macula. The macula, which is at the back of the eye, is responsible for clear vision. The abnormal blood vessels may leak fluid or blood into the eye and interfere with the macula's function, resulting in decreased vision.

##### How Beovu works

A substance called vascular endothelial growth factor A (VEGF-A) causes the growth of blood vessels in the eye. By attaching to VEGF-A, Beovu blocks its effect and so reduces the growth of abnormal blood vessels in AMD, which in turn reduces the leakage of fluid or blood in the eye.

Beovu may slow down disease progression and thereby maintain, or even improve, your vision.

## **2. What you need to know before you are given Beovu**

### **You must not be given Beovu:**

- if you are allergic to brolocizumab or any of the other ingredients of this medicine (listed in section 6).
- if you have an active or suspected infection in or around the eye.
- if you have pain or redness in your eye (eye inflammation).

If any of these applies to you, tell your doctor. You should not be given Beovu.

### **Warnings and precautions**

Talk to your doctor before you are given Beovu if any of the following applies to you:

- if you have glaucoma (an eye condition usually caused by high pressure in the eye).
- if you have a history of seeing flashes of light or floaters (dark floating spots) and if you have a sudden increase in the size and number of floaters.
- if you have had eye surgery in the last 4 weeks or if eye surgery is planned in the next four weeks.
- if you have ever had any eye diseases or eye treatments.

### **Tell your doctor immediately if you:**

- develop signs of a possible eye infection, such as redness of the eye, eye pain, increased discomfort, worsening eye redness, blurred or decreased vision, an increased number of small particles in your vision, increased sensitivity to light.
- develop sudden vision loss, which could be a sign of retinal artery occlusion.

Furthermore it is important for you to know that:

- the safety and efficacy of Beovu when administered to both eyes at the same time has not been studied and use in this way may lead to an increased risk of experiencing side effects.
- injections with Beovu may cause an increase in eye pressure (intraocular pressure) in some patients within 30 minutes of the injection. Your doctor will monitor this after each injection.
- your doctor will check whether you have other risk factors that may increase the chance of a tear or detachment of one of the layers at the back of the eye (retinal detachment or tear, and retinal pigment epithelial detachment or tear), in which case Beovu must be given with caution.

The systemic use of VEGF inhibitors, substances similar to those contained in Beovu, is potentially related to the risk of blood clots blocking blood vessels (arterial thromboembolic events), which may lead to heart attack or stroke. There is a theoretical risk of such events following injection of Beovu into the eye.

### **Children and adolescents**

Beovu is not used in children and adolescents, because wet AMD occurs only in adults.

### **Other medicines and Beovu**

Tell your doctor if you are using, have recently used or might use any other medicines.

### **Pregnancy and breast-feeding**

If you are pregnant or breast-feeding, think that you may be pregnant or are planning to have a baby, ask your doctor for advice before this medicine is given to you.

Breast-feeding is not recommended during treatment with Beovu and for at least one month after stopping treatment with Beovu because it is not known whether Beovu passes into human milk.

Women who could become pregnant must use an effective method of birth control during treatment and for at least one month after stopping treatment with Beovu. If you become pregnant or think you are pregnant during treatment, tell your doctor right away.

### **Driving and using machines**

After your injection with Beovu, you may have temporary vision problems (for example blurred vision). Do not drive or use machines as long as these last.

### **Beovu contains sodium**

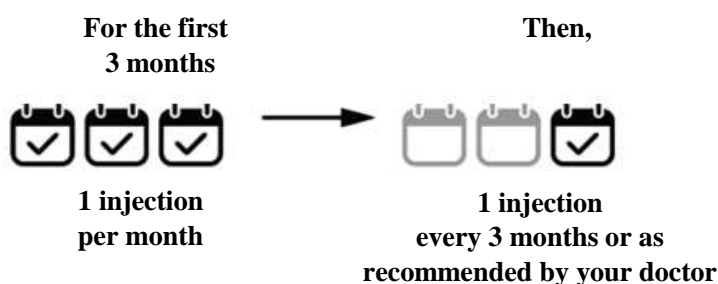
The medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially “sodium-free”.

## **3. How Beovu is given**

### **How much and how often Beovu is given**

The recommended dose is 6 mg brolucizumab.

- You will be treated with one injection every month for the first 3 months.
- After that, you may get one injection every 3 months. Your doctor will determine your treatment interval based on the condition of your eye; some patients may need treatment every 2 months.



### **Method of administration**

Beovu is given as an injection into your eye (intravitreal use) by an eye doctor.

Before the injection, your doctor will clean your eye carefully, to prevent infection. Your doctor will also give you an eye drop (local anaesthetic) to numb the eye to reduce or prevent pain from the injection.

### **How long does Beovu treatment last for**

Wet AMD is a chronic disease and it therefore needs long-term treatment with this medicine, possibly continuing for months or years. Your doctor will check that the treatment is working during your regular scheduled visits. Your doctor may also check on your eyes between injections. If you have questions about how long you will receive Beovu, talk to your doctor.

### **Before stopping Beovu treatment**

Speak with your doctor before stopping treatment. Stopping treatment may increase your risk of vision loss and your vision may worsen.

If you have any further questions on the use of this medicine, ask your doctor.



#### 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The side effects with Beovu injection are either from the medicine itself or from the injection procedure and they mostly affect the eye.

##### **Some side effects could be serious**

Get immediate medical help if you have any of the following, which are signs of allergic reactions, inflammations or infections:

- a sudden decrease or change in vision
- pain, increased discomfort, worsening eye redness

If you have any serious side effects, **tell your doctor immediately.**

##### **Other possible side effects**

Other side effects which may occur after Beovu treatment include those listed below.

Most of the side effects are mild to moderate and will generally disappear within a week after each injection.

If these side effects become severe, please tell your doctor.

##### **Common:** *may affect up to 1 in every 10 people*

- inflammation of the middle layer of the eye wall (uveitis)
- detachment of the gel-like substance inside the eye (vitreous detachment)
- tearing of the retina (the part at the back of the eye that detects light) or one of its layers (retinal pigment epithelial tear)
- reduced sharpness of vision (reduced visual acuity)
- bleeding in the retina (retinal haemorrhage)
- inflammation of the iris, the coloured part of the eye (iritis)
- clouding of the lens of the eye (cataract)
- bleeding from small blood vessels in the outer layer of the eye (conjunctival haemorrhage)
- moving spots in your vision (vitreous floaters)
- eye pain
- increase in pressure inside the eye (intraocular pressure increase)
- redness in the white of the eye (conjunctivitis)
- blurred or unclear vision
- scratched cornea, damage to the clear layer of the eyeball that covers the iris (corneal abrasion)
- damage to the clear layer of the eyeball that covers the iris (punctate keratitis)
- allergic reactions (hypersensitivity)

##### **Uncommon:** *may affect up to 1 in every 100 people*

- severe inflammation inside the eye (endophthalmitis)
- blindness
- sudden vision loss due to blockage of an artery in the eye (retinal artery occlusion)
- detachment of the retina (retinal detachment)
- redness of the eye (conjunctival hyperaemia)
- increased tear production (lacrimation increased)
- abnormal feeling in the eye
- detachment of one of the layers of the retina (detachment of retinal pigment epithelium)
- inflammation of the gel-like substance inside the eye (vitritis)
- inflammation of the front of the eye (anterior chamber inflammation or flare)
- inflammation in the iris and its adjacent tissue in the eye (iridocyclitis)
- swelling of the cornea, the clear layer of the eyeball (corneal oedema)
- bleeding in the eye (vitreous haemorrhage)

### **Reporting of side effects**

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in [Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

### **5. How to store Beovu**

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C).

Do not freeze.

Keep the pre-filled syringe in the sealed blister and in the outer carton in order to protect from light.

Prior to use, the unopened blister with the pre-filled syringe may be kept at room temperature (below 25°C) for up to 24 hours.

### **6. Contents of the pack and other information**

#### **What Beovu contains**

- The active substance is brolocizumab. One ml solution for injection contains 120 mg brolocizumab. Each pre-filled syringe contains 19.8 mg brolocizumab in 0.165 ml solution. This provides a usable amount to deliver a single dose of 0.05 ml solution containing 6 mg of brolocizumab.
- The other ingredients are: sodium citrate, sucrose, polysorbate 80, water for injections.

#### **What Beovu looks like and contents of the pack**

Beovu 120 mg/ml solution for injection in a pre-filled syringe (injection) is a clear to slightly opalescent, colourless to slightly brownish-yellow aqueous solution.

Pack size of 1 pre-filled syringe for single use only.

#### **Marketing Authorisation Holder**

Novartis Europharm Limited  
Vista Building  
Elm Park, Merrion Road  
Dublin 4  
Ireland

#### **Manufacturer**

S.A. ALCON-COUVREUR N.V.  
Rijksweg 14  
2870 Puurs  
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

**België/Belgique/Belgien**

Novartis Pharma N.V.  
Tél/Tel: +32 2 246 16 11

**България**

Novartis Bulgaria EOOD  
Тел.: +359 2 489 98 28

**Česká republika**

Novartis s.r.o.  
Tel: +420 225 775 111

**Danmark**

Novartis Healthcare A/S  
Tlf: +45 39 16 84 00

**Deutschland**

Novartis Pharma GmbH  
Tel: +49 911 273 0

**Eesti**

SIA Novartis Baltics Eesti filiaal  
Tel: +372 66 30 810

**Ελλάδα**

Novartis (Hellas) A.E.B.E.  
Τηλ: +30 210 281 17 12

**España**

Novartis Farmacéutica, S.A.  
Tel: +34 93 306 42 00

**France**

Novartis Pharma S.A.S.  
Tél: +33 1 55 47 66 00

**Hrvatska**

Novartis Hrvatska d.o.o.  
Tel. +385 1 6274 220

**Ireland**

Novartis Ireland Limited  
Tel: +353 1 260 12 55

**Ísland**

Vistor hf.  
Sími: +354 535 7000

**Italia**

Novartis Farma S.p.A.  
Tel: +39 02 96 54 1

**Lietuva**

SIA Novartis Baltics Lietuvos filialas  
Tel: +370 5 269 16 50

**Luxembourg/Luxemburg**

Novartis Pharma N.V.  
Tél/Tel: +32 2 246 16 11

**Magyarország**

Novartis Hungária Kft.  
Tel.: +36 1 457 65 00

**Malta**

Novartis Pharma Services Inc.  
Tel: +356 2122 2872

**Nederland**

Novartis Pharma B.V.  
Tel: +31 88 04 52 111

**Norge**

Novartis Norge AS  
Tlf: +47 23 05 20 00

**Österreich**

Novartis Pharma GmbH  
Tel: +43 1 86 6570

**Polska**

Novartis Poland Sp. z o.o.  
Tel.: +48 22 375 4888

**Portugal**

Novartis Farma - Produtos Farmacêuticos, S.A.  
Tel: +351 21 000 8600

**România**

Novartis Pharma Services Romania SRL  
Tel: +40 21 31299 01

**Slovenija**

Novartis Pharma Services Inc.  
Tel: +386 1 300 75 50

**Slovenská republika**

Novartis Slovakia s.r.o.  
Tel: +421 2 5542 5439

**Suomi/Finland**

Novartis Finland Oy  
Puh/Tel: +358 (0)10 6133 200

**Κύπρος**

Novartis Pharma Services Inc.  
Τηλ: +357 22 690 690

**Latvija**

SIA Novartis Baltics  
Tel: +371 67 887 070

**Sverige**

Novartis Sverige AB  
Tel: +46 8 732 32 00

**United Kingdom**

Novartis Pharmaceuticals UK Ltd.  
Tel: +44 1276 698370

**This leaflet was last revised in**

**Other sources of information**

Detailed information on this medicine is available on the European Medicines Agency web site:

<http://www.ema.europa.eu>

The following information is intended for healthcare professionals only:

### Instruction for use of pre-filled syringe

#### **Storage and inspection**



Store Beovu in the refrigerator (2°C - 8°C). Do not freeze. Keep the pre-filled syringe in its sealed blister and the outer carton in order to protect from light.



Prior to use, the unopened blister with the pre-filled syringe of Beovu may be kept at room temperature (below 25°C) for up to 24 hours. Make sure that your pack contains a sterile pre-filled syringe in a sealed blister. After opening the blister pack, proceed under aseptic conditions.



Beovu is a clear to slightly opalescent and colourless to slightly brownish-yellow aqueous solution.



The solution should be inspected visually upon removal from the refrigerator and prior to administration. If particulates or cloudiness are visible, the pre-filled syringe must not be used and appropriate replacement procedures followed.

The pre-filled syringe is sterile and for single use only. Do not use if the packaging or pre-filled syringe are damaged or expired.

#### **How to prepare and administer Beovu**

The pre-filled syringe contains more than the recommended dose of 6 mg. The extractable volume of the pre-filled syringe (0.165 ml) is not to be used in total. The excess volume should be expelled prior to injection. Injecting the entire volume of the pre-filled syringe could result in overdose.

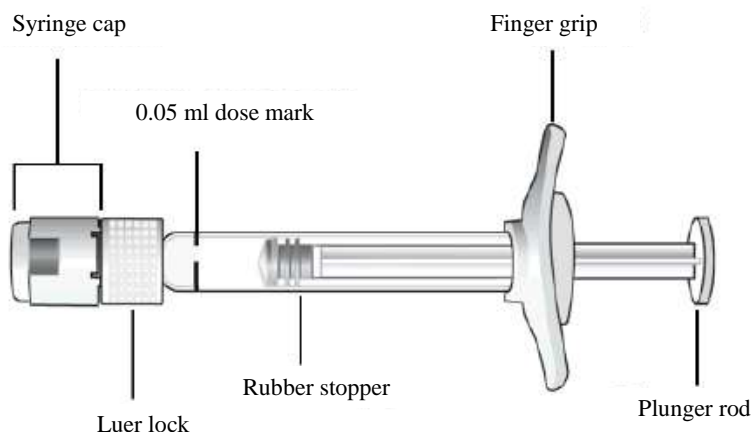
The intravitreal injection procedure must be carried out under aseptic conditions, which includes the use of surgical hand disinfection, sterile gloves, a sterile drape, a sterile eyelid speculum (or equivalent) and the availability of sterile paracentesis equipment (if required).

Adequate anaesthesia and a broad-spectrum topical microbicide to disinfect the periocular skin, eyelid and ocular surface should be administered prior to the injection.

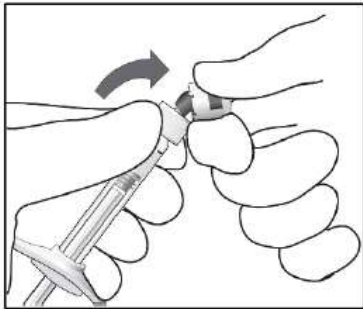
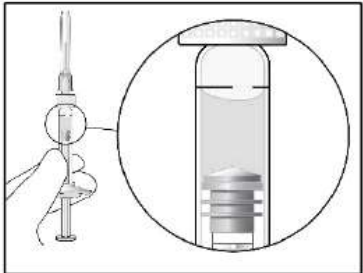
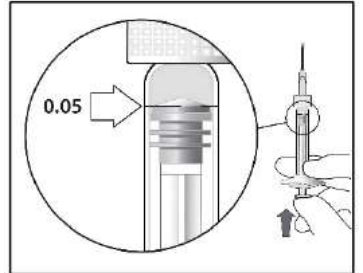
For intravitreal injection, use a 30G x ½" sterile injection needle. The injection needle is not included in the Beovu pack.

Ensure that the injection is given immediately after preparation of the dose (step 5).

**Note: The dose must be set to 0.05 ml.**



### Injection procedure

1.	Peel the lid off the syringe blister and, using aseptic technique, remove the syringe.
<p>2.</p> 	Snap off (do not turn or twist) the syringe cap.
3.	Aseptically and firmly assemble a 30G x 1/2" injection needle onto the syringe.
<p>4.</p> 	To check for air bubbles, hold the syringe with the needle pointing up. If there are any air bubbles, gently tap the syringe with your finger until the bubbles rise to the top. Carefully remove the needle cap by pulling it straight off.
<p>5.</p> 	Hold the syringe at eye level and carefully push the plunger until the edge below the dome of the rubber stopper is aligned with the 0.05 ml dose mark. This will expel the air and the excess solution and set the dose to 0.05 ml. The syringe is ready for the injection.
6.	Inject slowly until the rubber stopper reaches the end of the syringe to deliver the volume of 0.05 ml. Confirm delivery of the full dose by checking that the rubber stopper has reached the end of the syringe barrel.

Note: Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Commonly asked questions and answers

Q: What if I cannot remove all the air bubbles from the liquid?

A: It is important that the liquid is air free. However, tiny air bubbles that are attached to the stopper usually do not detach from the stopper during the injection and therefore do not affect the dose volume.

## Package leaflet: Information for the patient

### Beovu 120 mg/ml solution for injection brolucizumab

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

#### **Read all of this leaflet carefully before you are given this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

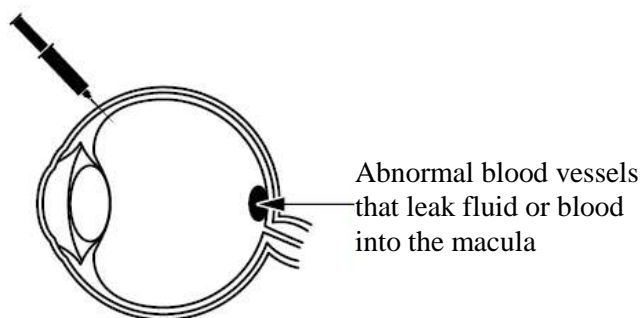
#### **What is in this leaflet**

1. What Beovu is and what it is used for
2. What you need to know before you are given Beovu
3. How Beovu is given
4. Possible side effects
5. How to store Beovu
6. Contents of the pack and other information

#### **1. What Beovu is and what it is used for**

##### **What Beovu is**

Beovu contains the active substance brolucizumab, which belongs to a group of medicines called antineovascularisation agents. Beovu is injected into the eye by your doctor to treat an eye disorder called neovascular (wet) age-related macular degeneration (AMD).



##### **What Beovu is used for**

Beovu is used to treat neovascular wet AMD in adults, which occurs when abnormal blood vessels form and grow underneath the macula. The macula, which is at the back of the eye, is responsible for clear vision. The abnormal blood vessels may leak fluid or blood into the eye and interfere with the macula's function, resulting in decreased vision.

##### **How Beovu works**

A substance called vascular endothelial growth factor A (VEGF-A) causes the growth of blood vessels in the eye. By attaching to VEGF-A, Beovu blocks its effect and so reduces the growth of abnormal blood vessels in AMD, which in turn reduces the leakage of fluid or blood in the eye.

Beovu may slow down disease progression and thereby maintain, or even improve, your vision.



## **2. What you need to know before you are given Beovu**

### **You must not be given Beovu:**

- if you are allergic to brolocizumab or any of the other ingredients of this medicine (listed in section 6).
- if you have an active or suspected infection in or around the eye.
- if you have pain or redness in your eye (eye inflammation).

If any of these applies to you, tell your doctor. You should not be given Beovu.

### **Warnings and precautions**

Talk to your doctor before you are given Beovu if any of the following applies to you:

- if you have glaucoma (an eye condition usually caused by high pressure in the eye).
- if you have a history of seeing flashes of light or floaters (dark floating spots) and if you have a sudden increase in the size and number of floaters.
- if you have had eye surgery in the last 4 weeks or if eye surgery is planned in the next four weeks.
- if you have ever had any eye diseases or eye treatments.

### **Tell your doctor immediately if you:**

- develop signs of a possible eye infection, such as redness of the eye, eye pain, increased discomfort, worsening eye redness, blurred or decreased vision, an increased number of small particles in your vision, increased sensitivity to light.
- develop sudden vision loss, which could be a sign of retinal artery occlusion.

Furthermore it is important for you to know that:

- the safety and efficacy of Beovu when administered to both eyes at the same time has not been studied and use in this way may lead to an increased risk of experiencing side effects.
- injections with Beovu may cause an increase in eye pressure (intraocular pressure) in some patients within 30 minutes of the injection. Your doctor will monitor this after each injection.
- your doctor will check whether you have other risk factors that may increase the chance of a tear or detachment of one of the layers at the back of the eye (retinal detachment or tear, and retinal pigment epithelial detachment or tear), in which case Beovu must be given with caution.

The systemic use of VEGF inhibitors, substances similar to those contained in Beovu, is potentially related to the risk of blood clots blocking blood vessels (arterial thromboembolic events), which may lead to heart attack or stroke. There is a theoretical risk of such events following injection of Beovu into the eye.

### **Children and adolescents**

Beovu is not used in children and adolescents, because wet AMD occurs only in adults.

### **Other medicines and Beovu**

Tell your doctor if you are using, have recently used or might use any other medicines.

### **Pregnancy and breast-feeding**

If you are pregnant or breast-feeding, think that you may be pregnant or are planning to have a baby, ask your doctor for advice before this medicine is given to you.

Breast-feeding is not recommended during treatment with Beovu and for at least one month after stopping treatment with Beovu because it is not known whether Beovu passes into human milk.

Women who could become pregnant must use an effective method of birth control during treatment and for at least one month after stopping treatment with Beovu. If you become pregnant or think you are pregnant during treatment, tell your doctor right away.

### **Driving and using machines**

After your injection with Beovu, you may have temporary vision problems (for example blurred vision). Do not drive or use machines as long as these last.

### **Beovu contains sodium**

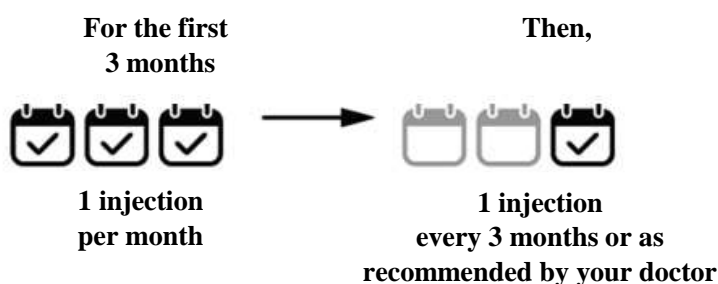
The medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially “sodium-free”.

## **3. How Beovu is given**

### **How much and how often Beovu is given**

The recommended dose is 6 mg brolucizumab.

- You will be treated with one injection every month for the first 3 months.
- After that, you may get one injection every 3 months. Your doctor will determine your treatment interval based on the condition of your eye; some patients may need treatment every 2 months.



### **Method of administration**

Beovu is given as an injection into your eye (intravitreal use) by an eye doctor.

Before the injection, your doctor will clean your eye carefully, to prevent infection. Your doctor will also give you an eye drop (local anaesthetic) to numb the eye to reduce or prevent pain from the injection.

### **How long does Beovu treatment last for**

Wet AMD is a chronic disease and it therefore needs long-term treatment with this medicine, possibly continuing for months or years. Your doctor will check that the treatment is working during your regular scheduled visits. Your doctor may also check on your eyes between injections. If you have questions about how long you will receive Beovu, talk to your doctor.

### **Before stopping Beovu treatment**

Speak with your doctor before stopping treatment. Stopping treatment may increase your risk of vision loss and your vision may worsen.

If you have any further questions on the use of this medicine, ask your doctor.

#### 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The side effects with Beovu injection are either from the medicine itself or from the injection procedure and they mostly affect the eye.

##### **Some side effects could be serious**

Get immediate medical help if you have any of the following, which are signs of allergic reactions, inflammations or infections:

- a sudden decrease or change in vision
- pain, increased discomfort, worsening eye redness

If you have any serious side effects, **tell your doctor immediately.**

##### **Other possible side effects**

Other side effects which may occur after Beovu treatment include those listed below.

Most of the side effects are mild to moderate and will generally disappear within a week after each injection.

If these side effects become severe, please tell your doctor.

##### **Common:** *may affect up to 1 in every 10 people*

- inflammation of the middle layer of the eye wall (uveitis)
- detachment of the gel-like substance inside the eye (vitreous detachment)
- tearing of the retina (the part at the back of the eye that detects light) or one of its layers (retinal pigment epithelial tear)
- reduced sharpness of vision (reduced visual acuity)
- bleeding in the retina (retinal haemorrhage)
- inflammation of the iris, the coloured part of the eye (iritis)
- clouding of the lens of the eye (cataract)
- bleeding from small blood vessels in the outer layer of the eye (conjunctival haemorrhage)
- moving spots in your vision (vitreous floaters)
- eye pain
- increase in pressure inside the eye (intraocular pressure increase)
- redness in the white of the eye (conjunctivitis)
- blurred or unclear vision
- scratched cornea, damage to the clear layer of the eyeball that covers the iris (corneal abrasion)
- damage to the clear layer of the eyeball that covers the iris (punctuate keratitis)
- allergic reactions (hypersensitivity)

##### **Uncommon:** *may affect up to 1 in every 100 people*

- severe inflammation inside the eye (endophthalmitis)
- blindness
- sudden vision loss due to blockage of an artery in the eye (retinal artery occlusion)
- detachment of the retina (retinal detachment)
- redness of the eye (conjunctival hyperaemia)
- increased tear production (lacrimation increased)
- abnormal feeling in the eye
- detachment of one of the layers of the retina (detachment of retinal pigment epithelium)
- inflammation of the gel-like substance inside the eye (vitritis)
- inflammation of the front of the eye (anterior chamber inflammation or flare)
- inflammation in the iris and its adjacent tissue in the eye (iridocyclitis)
- swelling of the cornea, the clear layer of the eyeball (corneal oedema)
- bleeding in the eye (vitreous haemorrhage)

### **Reporting of side effects**

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in [Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

### **5. How to store Beovu**

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C).

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Prior to use, the unopened vial may be kept at room temperature (below 25°C) for up to 24 hours.

### **6. Contents of the pack and other information**

#### **What Beovu contains**

- The active substance is brolocizumab. One ml solution for injection contains 120 mg brolocizumab. Each vial contains 27.6 mg brolocizumab in 0.23 ml solution. This provides a usable amount to deliver a single dose of 0.05 ml solution containing 6 mg of brolocizumab.
- The other ingredients are: sodium citrate, sucrose, polysorbate 80, water for injections.

#### **What Beovu looks like and contents of the pack**

Beovu 120 mg/ml solution for injection (injection) is a clear to slightly opalescent, colourless to slightly brownish-yellow aqueous solution.

Pack size of 1 vial and 1 blunt filter needle (18G x 1½", 1.2 mm x 40 mm, 5 µm) for single use only.

#### **Marketing Authorisation Holder**

Novartis Europharm Limited  
Vista Building  
Elm Park, Merrion Road  
Dublin 4  
Ireland

#### **Manufacturer**

S.A. ALCON-COUVREUR N.V.  
Rijksweg 14  
2870 Puurs  
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

**België/Belgique/Belgien**

Novartis Pharma N.V.  
Tél/Tel: +32 2 246 16 11

**България**

Novartis Bulgaria EOOD  
Тел.: +359 2 489 98 28

**Česká republika**

Novartis s.r.o.  
Tel: +420 225 775 111

**Danmark**

Novartis Healthcare A/S  
Tlf: +45 39 16 84 00

**Deutschland**

Novartis Pharma GmbH  
Tel: +49 911 273 0

**Eesti**

SIA Novartis Baltics Eesti filiaal  
Tel: +372 66 30 810

**Ελλάδα**

Novartis (Hellas) A.E.B.E.  
Τηλ: +30 210 281 17 12

**España**

Novartis Farmacéutica, S.A.  
Tel: +34 93 306 42 00

**France**

Novartis Pharma S.A.S.  
Tél: +33 1 55 47 66 00

**Hrvatska**

Novartis Hrvatska d.o.o.  
Tel. +385 1 6274 220

**Ireland**

Novartis Ireland Limited  
Tel: +353 1 260 12 55

**Ísland**

Vistor hf.  
Sími: +354 535 7000

**Italia**

Novartis Farma S.p.A.  
Tel: +39 02 96 54 1

**Lietuva**

SIA Novartis Baltics Lietuvos filialas  
Tel: +370 5 269 16 50

**Luxembourg/Luxemburg**

Novartis Pharma N.V.  
Tél/Tel: +32 2 246 16 11

**Magyarország**

Novartis Hungária Kft.  
Tel.: +36 1 457 65 00

**Malta**

Novartis Pharma Services Inc.  
Tel: +356 2122 2872

**Nederland**

Novartis Pharma B.V.  
Tel: +31 88 04 52 111

**Norge**

Novartis Norge AS  
Tlf: +47 23 05 20 00

**Österreich**

Novartis Pharma GmbH  
Tel: +43 1 86 6570

**Polska**

Novartis Poland Sp. z o.o.  
Tel.: +48 22 375 4888

**Portugal**

Novartis Farma - Produtos Farmacêuticos, S.A.  
Tel: +351 21 000 8600

**România**

Novartis Pharma Services Romania SRL  
Tel: +40 21 31299 01

**Slovenija**

Novartis Pharma Services Inc.  
Tel: +386 1 300 75 50

**Slovenská republika**

Novartis Slovakia s.r.o.  
Tel: +421 2 5542 5439

**Suomi/Finland**

Novartis Finland Oy  
Puh/Tel: +358 (0)10 6133 200

**Κύπρος**

Novartis Pharma Services Inc.  
Τηλ: +357 22 690 690

**Latvija**

SIA Novartis Baltics  
Tel: +371 67 887 070

**Sverige**

Novartis Sverige AB  
Tel: +46 8 732 32 00

**United Kingdom**

Novartis Pharmaceuticals UK Ltd.  
Tel: +44 1276 698370

**This leaflet was last revised in**

**Other sources of information**

Detailed information on this medicine is available on the European Medicines Agency web site:

<http://www.ema.europa.eu>

The following information is intended for healthcare professionals only:

### Instructions for use of vial

#### **Storage and inspection**



Store Beovu in the refrigerator (2°C - 8°C). Do not freeze. Keep the vial in the outer carton in order to protect from light.



Prior to use, the unopened vial of Beovu may be kept at room temperature (below 25°C) for up to 24 hours. After opening the vial, proceed under aseptic conditions.



Beovu is a clear to slightly opalescent and colourless to slightly brownish-yellow aqueous solution.



The solution should be inspected visually upon removal from the refrigerator and prior to administration. If particulates or cloudiness are visible, the vial must not be used and appropriate replacement procedures followed.

The contents of the vial and the filter needle are sterile and for single use only. Do not use if the packaging, vial and/or filter needle are damaged or expired.

#### **How to prepare and administer Beovu**

The vial contains more than the recommended dose of 6 mg. The extractable volume of the vial (0.23 ml) is not to be used in total. The excess volume should be expelled prior to injection. Injecting the entire volume of the vial could result in overdose.

The intravitreal injection procedure must be carried out under aseptic conditions, which includes the use of surgical hand disinfection, sterile gloves, a sterile drape and a sterile eyelid speculum (or equivalent) and the availability of sterile paracentesis equipment (if required).

Adequate anaesthesia and a broad-spectrum topical microbicide to disinfect the periocular skin, eyelid and ocular surface should be administered prior to the injection.

For preparation and intravitreal injection, the following single-use medical devices are needed:

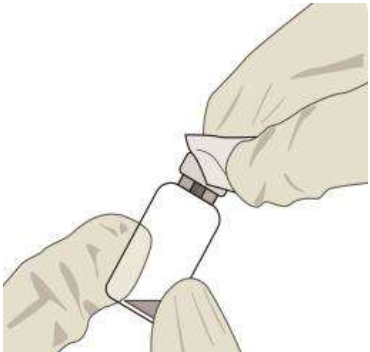
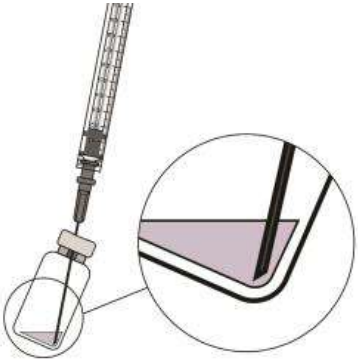

- A 30G x ½" injection needle, sterile.
- A 1 ml syringe with a 0.05 ml dose mark, sterile.
- The 5 µm blunt filter needle (18G x 1½", 1.2 mm x 40 mm), sterile.

The injection needle and the syringe are not included in the Beovu pack.

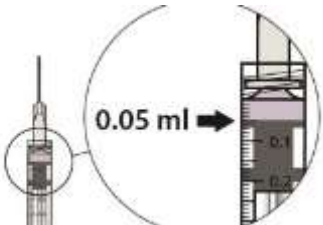
Ensure that the injection is given immediately after preparation of the dose (step 8).

**Note: The dose must be set to 0.05 ml.**

## Injection procedure

<p>1.</p> 	<p>Remove the vial cap and clean the vial septum (e.g. with 70% alcohol swab).</p>
<p>2.</p>	<p>Assemble the filter needle onto a 1 ml syringe using aseptic technique.</p>
<p>3.</p>	<p>Push the filter needle into the centre of the vial septum until the needle touches the bottom of the vial.</p>
<p>4.</p> 	<p>To withdraw the liquid, hold the vial slightly inclined and slowly withdraw all the liquid from the vial and filter needle. Ensure that the plunger rod is drawn sufficiently back when emptying the vial in order to completely empty the filter needle.</p>
<p>5.</p>	<p>Disconnect the filter needle from the syringe in an aseptic manner and dispose of it. The filter needle is not to be used for intravitreal injection.</p>
<p>6.</p>	<p>Aseptically and firmly assemble a 30G x 1/2" injection needle onto the syringe.</p>
<p>7.</p> 	<p>To check for air bubbles, hold the syringe with the needle pointing up. If there are any air bubbles, gently tap the syringe with your finger until the bubbles rise to the top.</p>



<p>8.</p> 	<p>Hold the syringe at eye level and carefully push the plunger to expel the air along with the excess solution from the syringe and adjust the dose to the 0.05 ml mark. The syringe is ready for the injection.</p>
<p>9.</p>	<p>Inject slowly until the rubber stopper reaches the end of the syringe to deliver the volume of 0.05 ml. Confirm delivery of the full dose by checking that the rubber stopper has reached the end of the syringe barrel.</p>

Note: Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Commonly asked questions and answers

Q: What if I have difficulty withdrawing sufficient liquid from the vial?

A: Do not shake the vial before withdrawal but let the liquid settle to the bottom of the vial. Ensure the vial is in an upright, slightly inclined position. **Slowly withdraw** the plunger and wait for the liquid to appear in the syringe barrel. Continue to withdraw slowly to completely empty the vial and the filter needle.

Q: What if I cannot remove all the air bubbles from the liquid?

A: It is important that the liquid is air free. However, tiny air bubbles that are attached to the stopper usually do not detach from the stopper during the injection and therefore do not affect the dose volume.