معلومات هامة لسلامة المرضى

# دليل المريض إلى العلاج باستخدام Beovu® (بيفاسيزوماب)

لعلاج الضمور البقعي الرطب
المرتبط بالعمر (إيه إم دي)
والوذمة البقعية السكرية

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Beovu EU RMP V 8.1 Jan 2023 SA2212076538

## ما هو الضمور البقعي الوعائي (الرطب) المرتبط بالعمر؟

يحدث الضمور البقعي الرطب المرتبط بالعمر عندما تتكون أوعية دموية غير طبيعية وتنمو تحت البقعة. البقعة، التي توجد بالجزء الخلفي من العين، هي المسؤولة عن الرؤية الواضحة. قد تُسرب الأوعية الدَّموية غير الطبيعية السوائل أو الدم إلى العين وتتداخل مع وظيفة البقعة، الأمر الذي يُؤدي إلى انخفاض الرؤية.

## ما هي الوذمة البقعية السكرية (DME)؟

الوذمة البقعية السكرية هي مرض تصاعدي يسببه مرض السكري، وقد يؤدي إلى فقدان البصر أو العمى. قد ترشح الأوعية الدَّموية التالفة في العين سائلًا في البقعة. البقعة هي المسؤولة عن الرؤية المركزية وهي الجزء من العين الذي يُستَخدَم لفعل أمور مثل القراءة والقيادة والتعرف على الوجوه.



## لماذا وُصِف لي Beovu؟

يحتوي Beovu على المادة الفعَّالة برولوسيزوماب، التي تنتمي إلى مجموعة من الأدوية تُسمَّى مضادات التَّوَعِّي الحَديث.
تُسبِّب مادة تُسمَّى عامل النمو البطاني الوعائي أ (VEGF A) نمو الأوعية الدَّموية في العين.

يمنع Beovu تأثير المادة المُسمَّاة بعامل النمو البطاني الوعائي أ عن طريق الارتباط بها، وبالتَّالي يقلل من نمو الأوعية الدَّموية غير الطبيعية في حالات الضمور البقعي الرطب المرتبط بالعمر والوذمة البقعية السكرية؛ الأمر الذي بدوره يقلل من تسريب السوائل أو الدَّم في العين.

## كيف يُعطَى Beovu؟

- يحقن طبيبك Beovu في عينك (حَقْن داخل الجسم الزجاجي للعين)
- سيُجري لك طبيبك بعض اختبارات العين بعد حَقْنك. قد تشمل هذه الاختبارات قياس الضغط داخل عينك أو تقييم حالة عصبك البصري.

## ما المُتوَقَّع بعد العلاج؟

في بعض الأحيان، بعد الحَقْن داخل الجسم الزجاجي للعين كما هو الحال مع Beovu®، قد يحدث ما يلي:

- التهاب غير شائع ولكنه شديد (التهاب باطن المقلة)، مرتبط عادةً بحدوث عدوى داخل العين أو انفصال للطبقات الموجودة في الجزء الخلفي من العين (انفصال الشبكية/تمزُّقها)
- ارتفاع مؤقت في ضغط العين (الضغط داخل العين)، وهو أمر شائع ولكنه عادةً يكون بدون أعراض؛ يجب على الطبيب إجراء قياسات للضغط داخل العين لاكتشاف ذلك

## كيف يُعطَى Beovu؟

- قد يحدث التهاب بالأوعية الدَّموية الموجودة في الشبكية و/أو انسداد بالأوعية الدموية للعين (انسداد وعائي شبكي)، أو التهاب أقل شدة بالعين (التهاب باطن العين). قد يزداد خطر الإصابة بالسابق إذا كنت من أصل ياباني أو إذا كنتِ أنثى

- إذا أُصِبت بالتهاب باطن العين و/أو انسداد وعائي شبكي خلال العام الماضي، فأنت أكثر عرضة للإصابة بالتهاب الأوعية الدَّموية الموجودة في الشبكية و/أو الانسداد الوعائي الشبكي

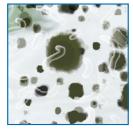
- من الممكن أيضًا حدوث رد فعل مناعي (استجابة مناعية).



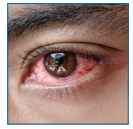
## ما المُتوَقَّع بعد العلاج؟ (تابع)

اطلب المساعدة الطبية فورًا إذا تعرَّضت لأيٍّ مما يلي:

انخفاض أو تغيُّر مفاجئ في حدة الرؤية



عدد جديد أو متزايد من العوائم
(جسيمات صغيرة تظهر في مجال الرؤية)



احمرار كلي في العين

ألم جديد أو مستمر بالعين أو تفاقم الشعور غير المريح بالعين

ومضات من الضوء أو زيادة الحساسية تجاه الضوء
(شعور بالانزعاج من الأضواء الساطعة)

## ما الذي يمكنني فعله بعد علاجي؟

- بعد الحَقْن، قد تتأثر رؤيتك مؤقتًا (على سبيل المثال: عدم وضوح الرؤية). لا تقم بممارسة القيادة أو استخدام الآلات طالما استمرت هذه الآثار الجانبية.
- كن سبَّاقًا وأخبر طبيبك أو ممرضتك إذا لاحظت أيَّة تغيُّرات في رؤيتك.
- من المهم اتباع جدول مواعيد الزيارات الذي أوصى به طبيبك.

**BEOVU**

**Important note:** Before prescribing, consult full prescribing information.

**Presentation:** Solution for injection. Each vial contains 27.6 mg of brolucizumab in 0.23 mL solution. Each pre-filled syringe contains 19.8 mg of brolucizumab in 0.165 mL solution.

**Indications:** Beovu is indicated for the treatment of

- neovascular (wet) age-related macular degeneration (AMD).
- visual impairment due to diabetic macular oedema (DME).

**Dosage regimen and administration:**

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

Posology

*Wet AMD*

The recommended dose is 6 mg brolucizumab (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 (see sections 4.4 and 5.1).

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

*DME*

The recommended dose is 6 mg brolucizumab (0.05 ml solution) administered by intravitreal injection every 6 weeks for the first 5 doses. Thereafter, the physician may individualise treatment intervals based on disease activity as assessed by visual acuity and/or anatomical parameters. 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.

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 brolucizumab).

*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 brolucizumab).

**Contraindications:** ♦Hypersensitivity to the active substance or to any of the excipients.

♦Active or suspected ocular or periocular infection. ♦Active intraocular inflammation.

**Warnings and precautions:**

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.

Endophthalmitis, intraocular inflammation, traumatic cataract, retinal detachment, retinal tear, retinal vasculitis, and/or retinal vascular occlusion

Intravitreal injections, including those with Beovu, have been associated with endophthalmitis, intraocular inflammation, traumatic cataract, retinal detachment and retinal tear (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 inflammation, including retinal vasculitis and/or retinal vascular occlusion

Intraocular inflammation, including retinal vasculitis and/or retinal vascular occlusion, has been reported with the use of Beovu (see sections 4.3 and 4.8). A higher number of intraocular inflammation events were observed among patients with treatment-emergent antibodies. After investigation, retinal vasculitis and/or retinal vascular occlusion were found to be immune-mediated events. Intraocular inflammation, including retinal vasculitis and/or retinal vascular occlusion, may occur following the first intravitreal injection and at any time of treatment. These events were observed more frequently at the beginning of the treatment.

Based on clinical studies these events were more frequent in female patients treated with Beovu than male patients (e.g. 5.3% females vs. 3.2% males in HAWK and HARRIER) and in Japanese patients.

In patients developing these events, treatment with Beovu should be discontinued and the events should be promptly managed. Patients treated with Beovu with a medical history of intraocular inflammation and/or retinal vascular occlusion (within 12 months prior to the first brolucizumab injection) should be closely monitored, since they are at increased risk of developing retinal vasculitis and/or retinal vascular occlusion.

The interval between two Beovu doses during maintenance treatment should not be less than 8 weeks considering that a higher incidence of intraocular inflammation (including retinal vasculitis) and retinal vascular occlusion was reported in patients with nAMD who received Beovu every 4 week maintenance dosing in a clinical study compared to patients who received Beovu every 8 or 12 week maintenance dosing in the pivotal Phase III clinical studies.

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 brolucizumab (see section 4.8). Special precaution is needed in patients with poorly controlled glaucoma (do not inject Beovu while the intraocular pressure is ≥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 brolucizumab administered in both eyes concurrently have not been studied.

Immunogenicity

As this is a therapeutic protein, there is a potential for immunogenicity with brolucizumab (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. Brolucizumab 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 ≥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 ≥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 brolucizumab 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 and DME 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".

Populations with limited data

There is limited experience with Beovu treatment in diabetic patients with HbA1c greater than 10% or with proliferative diabetic retinopathy. There is also no experience of treatment with Beovu in diabetic patients with uncontrolled hypertension. This lack of information should be considered by the physician when treating such patients.

**Pregnancy, lactation, females and males of reproductive potential**

Women of childbearing potential

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

Pregnancy

There are no or limited amount of data from the use of brolucizumab in pregnant women. A study in pregnant cynomolgus monkeys did not indicate any harmful effects with respect to reproductive toxicity. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3). Although the systemic exposure after ocular administration is very low due to its mechanism of action, there is a potential risk to embryofoetal development. Therefore, brolucizumab should not be used during pregnancy unless the potential benefit outweighs the potential risk to the foetus.

Breast-feeding

It is unknown whether brolucizumab is excreted in human milk. In a reproductive toxicity study, brolucizumab was not detected in the maternal milk or infant serum of cynomolgus monkeys (see section 5.3). A risk to the breast-fed newborn/infant cannot be excluded.

Brolucizumab 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 brolucizumab. A decision must be made whether to discontinue breast-feeding or to abstain from brolucizumab 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.

**Adverse drug reactions:**

Summary of the safety profile

*Wet AMD*

For wet AMD, a total of 1,088 patients treated with brolucizumab constituted the safety population in two Phase III studies. Of these, 730 patients were treated with the recommended dose of 6 mg.

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%).

*DME*

For DME, a total of 558 patients treated with brolucizumab constituted the safety population in two Phase III studies. Of these, 368 patients were treated with the recommended dose of 6 mg.

The most frequently reported adverse reaction was conjunctival haemorrhage (5.7%).

The most serious adverse reactions were retinal artery occlusion (0.5%) and endophthalmitis (0.3%).

Tabulated list of adverse reactions

The adverse reactions experienced following administration of Beovu in clinical studies are summarised in Table 1 below.

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 (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

**Table 1 Frequencies of adverse reactions in clinical studies and post-marketing experience**

| MedDRA System organ class | Frequency category |
|---|---|
| **Immune system disorders** | |
| Hypersensitivity (including urticaria, rash, pruritus, erythema) | Common |
| **Eye disorders** | |
| 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 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 |
| Retinal vascular occlusion | Uncommon |
| Retinal vasculitis | Uncommon |

Description of selected adverse reactions

*Immunogenicity*

There is a potential for an immune response in patients treated with Beovu.

*Wet AMD*

After dosing with Beovu for 88 weeks, treatment-emergent anti-brolucizumab antibodies were detected in 23–25% of patients.

*DME*

After dosing with Beovu for 52 weeks, treatment-emergent anti-brolucizumab antibodies were detected in 12-18% of patients.

Among AMD and DME patients with treatment-emergent antibodies, a higher number of intraocular inflammation adverse reactions were observed. After investigation, retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, were found to be immune-mediated adverse events related to exposure to Beovu (see section 4.4). 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 and DME. There were no major notable differences between the groups treated with brolucizumab and comparator.

**Interactions:** No formal interaction studies have been performed.

**Packs and prices:** Country specific

**Legal classification:** Country specific

**NSS version number:** SA_v2.1_NSS_Beovu_Oct2022

**Leaflet revision date:** Approved by EMA in 03/2022

# كيفية الاتصال بعيادة رعاية العين:

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