Understanding ranibizumab biosimilar: Ongavia®▼

Scope

Ongavia®▼is a licensed ranibizumab biosimilar available from Teva UK. The Welsh Medicines Advice Service (WMAS) supports the introduction of Ongavia®▼(ranibizumab) biosimilar by providing information for healthcare professionals involved in the procurement, storage, supply and administration of Ongavia®▼such as Ophthalmology medical and nursing specialists, and pharmacy teams**.**

Please note that:

- We do not cover the legal authority and regulatory framework under which medicines are administered to patients.
- It is advised that the information below is used in conjunction with the information provided by Teva UK in the Summary of Product Characteristics (SmPC) for Ongavia®▼**.**

Purpose

To support the introduction of Ongavia®▼(ranibizumab) biosimilar into clinical use, WMAS:

- summarises information relating to Ongavia®▼(ranibizumab) biosimilar in relation to the originator product Lucentis® and other anti-vascular endothelial growth factor (anti-VEGF) medicines, that specialist Ophthalmology medical and nursing staff, and pharmacy teams may wish to consider when preparing to use Ongavia®▼biosimilar.

- provides detailed information about:
    - similarities and differences between Ongavia®▼(ranibizumab) biosimilar and the originator product Lucentis® for licensed indications and product information; including how to prepare the dose of Ongavia®▼for intravitreal administration.

- provides high level information about:
    - evidence supporting use of Ongavia®▼biosimilar, signposting to relevant specialist information sources including guidance issued by the Royal College of Ophthalmologists and NICE.
    - characteristics of similar agents currently in use in the form of a comparison table.

Contents

Based on original work by Sarah Fenner, Specialist MI Pharmacist, Midlands and East Medicines Advice Service (Midlands site) & UK Drugs in Lactation Advisory Service · Published 26 May 2022, Specialist Pharmacy Service.

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1. Licensed indications

Ongavia® ▼ is licensed in adults for the treatment of:

- neovascular (wet) age-related macular degeneration (AMD)
- proliferative diabetic retinopathy (PDR)
- visual impairment due to diabetic macular oedema (DME)
- visual impairment due to choroidal neovascularisation (CNV)
- visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO).

These are the same licensed indications in adults as the originator product, Lucentis®.

2. Product Information

a. Presentation

Ongavia®▼ 10mg in 1mL solution for injection.

Each Ongavia®▼ vial contains 2.3mg of ranibizumab in 0.23mL solution.

The originator product Lucentis® is available as:

- **10mg in 1mL solution for injection (vial)** containing 2.3mg ranibizumab in 0.23mL solution.
- **10mg in 1mL solution for injection (pre-filled syringe)** containing 1.65mg ranibizumab in 0.165mL solution.

b. Dose

The dosing regimen for Ongavia®▼ is the same as Lucentis®.

The recommended dose in adults for Ongavia®▼ is 0.5mg, corresponding to an injection volume of 0.05mL, given as a single intravitreal injection.

Initiation of treatment: One injection per month until maximum visual acuity is achieved and/or there are no signs of disease activity. Three or more consecutive monthly injections may be needed. Leave at least four weeks between two doses injected into the same eye.

Maintenance of treatment: When maximum visual acuity is achieved and/or there are no signs of disease activity, treatment intervals can be extended stepwise until signs of disease activity or visual impairment recur.

- Wet AMD - treatment intervals should be extended by no more than two weeks at a time.
- DME - treatment intervals may be extended to up to one month at a time.
- PDR and RVO - treatment intervals may be gradually extended, however there are insufficient data to conclude on the length of these intervals.

If disease activity recurs, the treatment interval should be shortened accordingly.

The treatment of visual impairment due to CNV should be determined individually per patient based on disease activity. Some patients may only need one injection during the first 12 months; others may need more frequent treatment, including a monthly injection.

c. Excipients

Ongavia®▼ contains the same excipients as Lucentis®:

- α,α-trehalose dihydrate
- Histidine hydrochloride, monohydrate
- Histidine
- Polysorbate 20
- Water for injections

d. Storage and stability

Ongavia®▼ has the same storage conditions as Lucentis®

- Store in a refrigerator (2°C – 8°C)
- Keep the vial in the outer carton in order to protect from light
- Prior to use the unopened product may be kept at room temperature (25°C) for up to 24 hours.

Ongavia®▼ has a shelf life of **2 years**. Lucentis® products have a shelf life of **3 years**.

e. Preparing a dose

i. Equipment

The following items are required to prepare the Ongavia®▼ for intravitreal administration. They are not provided with the product and should be sourced locally.

- 5 micron filter needle (18G)
- 1mL sterile syringe (with a 0.05mL mark)
- sterile injection needle (30G x ½").

ii. Process

Full details on preparing Ongavia®▼intravitreal injection are available in the SmPC. A training video from the manufacturers can be accessed here *hyperlink once video available*. Further diagrams can be found here. Further information to follow.

Pre-injection preparation should be carried out in line with local and national guidelines, including the Royal College of Ophthalmologists intravitreal injection therapy guidance.

iii. Preparing Ongavia®▼ intravitreal injection

The vial is for single use only. Do not use vials that show signs of damage or tampering. Sterility cannot be guaranteed unless the packaging seal is intact.

1. Disinfect the outer part of the rubber stopper of the vial as per guidance.
2. Assemble a 5 micron filter needle (18G x 1 ½", 1.2mm x 40 mm) onto a 1mL syringe using aseptic technique.
3. Push the blunt filter needle into the centre of the vial stopper until the needle touches the bottom edge of the vial.
4. Withdraw all the liquid from the vial, ensuring the vial is kept in the upright position, slightly inclined to ease the complete withdrawal of liquid.
5. Draw back the plunger rod sufficiently when emptying the vial in order to completely empty the filter needle.
6. Leave the blunt filter needle in the vial and disconnect the syringe from the blunt filter needle.
7. **Discard the filter needle after withdrawal of the vial contents and do not use for intravitreal injection.**
8. Aseptically, and firmly, assemble an injection needle (30G x ½", 0.3mm x 13mm) onto the syringe.

9. Grip the hub of the injection needle whilst carefully removing the cap without disconnecting the injection needle from the syringe.
10. **There will be excess volume in the vial. Carefully expel any air and adjust the syringe volume to the required dose of 0.05mL. Discard the excess volume**.
11. Inspect the syringe visually for any particulate matter and/or discoloration prior to administration. Discard if any is seen.
12. The syringe is ready for injection.

f. After administration

- Do not recap the needle or detach it from the syringe.
- Dispose of the used syringe together with the needle in a sharps disposal container or in accordance with local requirements.
- Discard any unused product as per local process.

Healthcare professionals are reminded of the importance of reporting suspected adverse drug reactions to the Yellow Card scheme. For black triangle medicines such as Ongavia®▼, all suspected reactions should be reported, regardless of their severity.

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3. Evidence supporting safety and efficacy of Ongavia®▼ intravitreal injection

A randomised trial in patients with newly diagnosed treatment-naïve neovascular (wet) AMD (n=477) showed that the ranibizumab biosimilar (Ongavia®▼) was clinically equivalent to the reference product when 0.5mg was given by intravitreal injection every 4 weeks for up to 12 months.

The primary outcome was change from baseline BCVA (best-corrected visual acuity) at 8 weeks before the third injection was given. Equivalence was defined as a margin of 3 Early Treatment Diabetic Retinopathy Study (ETDRS) letters. The assessment of BCVA at 8 weeks has been endorsed by the regulatory authorities as being appropriate.

In the European relevant population of 429 patients ranibizumab biosimilar (Ongavia®▼) and reference ranibizumab (Lucentis®) showed mean improvements of +5.2 and +6.0 ETDRS letters respectively; an adjusted difference of 0.7 letters with a 95% confidence interval ranging between -2.3 to +0.9.

These results support ranibizumab biosimilar (Ongavia®▼) equivalence to the reference product.

The frequency and type of ocular adverse effects and immunogenicity were similar.

4. NICE recommendations

NICE recommends ranibizumab as a treatment option for:

- diabetic macular oedema
- choroidal neovascularisation associated with pathological myopia
- visual impairment caused by macular oedema secondary to retinal vein occlusion

NICE guidance on treatment of age-related macular degeneration published in 2018 states that no clinically significant differences in effectiveness and safety of aflibercept, bevacizumab and ranibizumab were seen in the trials considered. Therefore, comparable regimes will be more cost effective if the agent has lower net acquisition, administration and monitoring costs.

None of the available anti-VEGF medicines are currently recommended by NICE for the treatment of diabetic retinopathy. NICE was unable to make a recommendation on ranibizumab for treating diabetic retinopathy as the manufacturers did not submit any supporting evidence. NICE guidance on the management and monitoring of diabetic retinopathy is currently in development (publication expected April 24).

Where NICE has already recommended the originator biological medicine, the same guidance will normally apply to the biosimilar. Biosimilars do not require a separate or additional Technology Appraisal.

5. Royal College of Ophthalmologists

Guidance from the Royal College of Ophthalmologists on Age Related Macular Degeneration Services published in 2021 highlights that whilst ranibizumab was the first licensed anti-VEGF treatment for neovascular AMD, many centres switched to using aflibercept as first-line therapy following NICE approval in 2013.

Aflibercept's treatment schedule of three initial loading doses followed by bimonthly treatment in the first year, reduced the need for monthly review appointments in comparison to ranibizumab.

The choice of first-line agent may be further guided by service setup, locally agreed costs and local audit of treatment results.

6. Considerations for implementation

Formulation and preparation

Lucentis® (ranibizumab), Eylea® (aflibercept) and Beovu® (brolucizumab) are anti-VEGF medicines available as pre-filled syringes. Ongavia®▼ however, requires preparation prior to administration and this will need to be considered when planning clinic time. Staff training may also need to be considered.

Switching between Eylea® and Ongavia®▼

Both Ongavia®▼ and Eylea® (aflibercept) are anti-VEGF medicines. They have different indications, doses and treatment intervals. This is important to consider when planning clinic capacity, particularly if patients are switched from Eylea® to Ongavia®▼.

Table 1. Comparison of available anti-VEGF agents

	Lucentis®	Ongavia® ▼	Eylea®	Beovu®
Name of medicine	Ranibizumab	Ranibizumab	Aflibercept	Brolucizumab
Presentation	Vial and pre-filled syringe	Vial	Vial and pre-filled syringe	Pre-filled syringe
Licensed indications (in adults)	• Neovascular (wet) AMD • PDR • Visual impairment due to DME • Visual impairment due to CNV • Visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO)	• Neovascular (wet) AMD • PDR • Visual impairment due to DME • Visual impairment due to CNV • Visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO)	• Neovascular (wet) AMD • Visual impairment due to DME • Visual impairment due to CNV • Visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO)	• Neovascular (wet) AMD • Visual impairment due to DME
Dose	One injection (0.5mg) Consult the product literature for dosing intervals	One injection (0.5 mg) Consult the product literature for dosing intervals	One injection (2mg) Consult the product literature for dosing intervals	One injection (6 mg) Consult the product literature for dosing intervals
Storage	Store in a refrigerator (2-8°C) Prior to use, the unopened product may be kept at room temperature (25 ºC) for up to 24 hours Keep the product in the outer carton in order to protect from light	Store in a refrigerator (2-8°C) Prior to use, the unopened product may be kept at room temperature (25 ºC) for up to 24 hours Keep the vial in the outer carton in order to protect from light	Store in a refrigerator (2°C to 8°C). Unopened product may be kept at room temperature (below 25 ºC) for up to 24 hours Keep the product in the outer carton in order to protect from light	Store in a refrigerator (2°C - 8°C). The unopened product may be kept at room temperature (below 25°C) for up to 24 hours. Keep pre-filled syringe in its sealed blister and in the outer carton in order to protect from light.
Shelf life	3 years	2 years	2 years	2 years

	Lucentis®	Ongavia®▼	Eylea®	Beovu®
Adverse effects	**Ocular: (most frequent)** eye pain, ocular hyperaemia, increased intraocular pressure, vitritis, vitreous detachment, retinal haemorrhage, visual disturbance, vitreous floaters, conjunctival haemorrhage, eye irritation, foreign body sensation in eyes, increased lacrimation, blepharitis, dry eye and eye pruritus. **Non-ocular: (most frequent)** headache, nasopharyngitis, arthralgia. **Serious:** endophthalmitis, blindness, retinal detachment, retinal tear and iatrogenic traumatic cataract.	**Ocular: (most frequent**) eye pain, ocular hyperaemia, increased intraocular pressure, vitritis, vitreous detachment, retinal haemorrhage, visual disturbance, vitreous floaters, conjunctival haemorrhage, eye irritation, foreign body sensation in eyes, increased lacrimation, blepharitis, dry eye and eye pruritus. **Non-ocular**: **(most frequent)** headache, nasopharyngitis and arthralgia. **Serious:** endophthalmitis, blindness, retinal detachment, retinal tear and iatrogenic traumatic cataract.	**Ocular: (most frequent)** conjunctival or retinal haemorrhage, visual acuity reduced, eye pain, cataract, intraocular pressure increased, vitreous detachment, and vitreous floaters. **Serious:** blindness, endophthalmitis, retinal detachment, cataract traumatic, cataract, vitreous haemorrhage, vitreous detachment, and intraocular pressure increased.	**Ocular: (most frequent)** reduced visual acuity, cataract, conjunctival haemorrhage, vitreous floaters. **Serious:** blindness, endopthalmitis, retinal artery occlusion and retinal detachment.

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