Appendix 2: FAQs

1. The COLUMBUS-AMD clinical trial comparing safety and efficacy of biosimilar ranibizumab to reference product was only undertaken in patients with wet AMD. Is there evidence for use of biosimilar for its other licensed indications?

No - However since a biosimilar is highly similar to its reference product and this has been proved in one indication, its approval may be extrapolated to additional indications that are already approved for the reference medicine. This avoids the unnecessary repetition of clinical trials.

Ongavia® demonstrated clinical equivalence to the reference product, from the results of the COLUMBUS-AMD[1] trial and further clinical trials are underway for indications other than wet AMD.

Experience of use with biosimilars has shown that switching between a biosimilar and its reference medicine does not appear to impact efficacy, safety or immunogenicity.[2]

2. NICE TA 155 for ranibizumab relates to reference medicine Lucentis®. Is a separate TA required for biosimilar?

No - Where NICE has already recommended the originator biological medicine, the same guidance will apply to the biosimilar. Biosimilars do not required a separate or additional Technology Appraisal.

Specialist Pharmacy Service (SPS) has provided resources to support implementation of ranibizumab biosimilar.[3,4,5]
https://www.sps.nhs.uk/medicines/ranibizumab/

3. The ranibizumab biosimilar Summary of Product Characteristics (SPC)[6] states that 'Ongavia® must be administered by a qualified ophthalmologist experienced in intravitreal injections'. Clinics may use trained nurses to administer Lucentis® pre-filled syringe, so will they be able to administer Ongavia® or require additional training or supervision?

Lucentis® SPC[7] also recommends that *'Lucentis must be administered by a qualified ophthalmologist experienced in intravitreal injections'*. However, in practice this may be administered by a suitably trained HCP and RCOphth[8] guidance acknowledges this and recommends that '*it is essential that the HCP always has immediate access to advice from an ophthalmologist whilst giving injections and an appropriately trained clinician is available on site to deal with any very urgent complications'*

Intravitreal injections performed by the HCP will be 'off-label' for both Lucentis® and Ongavia®.

Services should ensure that intraocular injections are given by suitably trained healthcare professionals, such as:

- medical specialists i.e. ophthalmologists
- nurse practitioners, optometrists and technicians with experience in giving intraocular injections.

If the injection is delivered by someone who is not medically qualified, ensure that cover is in place to manage any ophthalmological or medical complications.

4. Are biosimilars of the same reference product interchangeable as for generic medicines?

No - A generic medicine is an exact copy of a chemically synthesised licensed medicine and as such, generic medicines are directly interchangeable with their reference medicine.
A biosimilar medicine is a highly similar copy of its reference medicine. Since it is not possible to replicate biological medicines exactly, a small degree of variation is expected.
This is also the case for biological medicines which show a small degree of expected variation within their molecular structures. This occurs even between batches of the same product and is due to the variability of biological systems and manufacturing processes.

5. The ranibizumab biosimilar vial is not supplied with syringes and needles. Are the recommended syringes and needles validated for intraocular use?

No – However the biosimilar and the Lucentis® brand of the vial have the same method of administration and the same needle requirements. The needles are recommended by the manufacturers as stated below for intravitreal use.

Ongavia® brand[6]:

The SPC for Ongavia® (biosimilar of ranibizumab) explains in section 6.6 that for preparation and intravitreal injection the following medical devices for single use are needed:

- a 5µm filter needle (18G)

- a 1 ml sterile syringe (including a 0.05 ml mark) and an injection needle (30G x ½″), for adult patients

Retinal specialists have recognised that all syringes used for intravitreal injections have limitations and that forthcoming products are coming closer to meeting "ideal" criteria.[9]

6. What is the risk of using syringes and needles that are not validated for intravitreal use?

BD issued a Field Safety Notice (FSN)[10] in 2021 advising that when syringes and needles are used for intraocular injections, the potential exists for "floaters" in patients' eyes which are believed to be due to silicone. (Note: Syringes and needles manufactured by BD have silicone applied to the inside of the barrels to provide lubrication for the plunger stopper, allowing it to move easily). The potential hazard is deposition of silicone oil (SO) droplets in the vitreous. The potential harm could be symptomatic "floaters" in the patient's field of vision which, normally, are tolerable and resolve over a few months. However, if sufficiently bothersome, floaters may lead to a vitrectomy for their removal.

SPS[11] issued a subsequent interim position statement in May 2021 and RCOphth[12] clarified their position, advising that they considered '*the risk to patients from delays to treatment because of this issue outweigh the risks of utilising the products highlighted in the FSN'.*

In 2022 Manchester Royal Eye Hospital (MREH) clinical team undertook a thorough risk assessment of using BD syringes and needles for intravitreal administration.

Following consultation following actions were agreed:

- The SOP for intraocular injections should include the following 'Immediately prior to the intraocular administration of a drug within a BD syringe, the contents of the syringe should be checked for the presence of visible particulate matter. Administration should only proceed if no visible particles are observed.'
- Syringes containing intraocular injections should not be agitated before use and specifically that they should not be flicked in order to remove air.
- If there are any concerns of complications as a result of the use of BD syringes for intraocular administration, these should be reported via the Trust Critical Incident Reporting System and MHRA Yellow Card Reporting System

7. What is the risk of endophthalmitis of administration of intravitreal injection from a vial vs a pre-filled syringe?

Intravitreal injection is considered a routine procedure[8] and endophthalmitis is a very rare occurrence with an incidence in the UK of approximately 0.02-0.06%.[15]

Where the drug is only presented in a vial (e.g. faricimab or biosimilar ranibizumab), HCPs will need to draw up the required dose of medicine into a syringe at the point of administration. Retrospective studies[13,14] comparing the risk of post-injection endophthalmitis with the use of prefilled syringes vs drawing up from a vial during intravitreal injection of ranibizumab have demonstrated a reduced risk with prefilled syringes.

The consequences of endophthalmitis can be severe and RCOphth provides recommendations to minimise risk in practice.[8,15]

8. Could aseptic services be used to compound vial into pre-filled syringe?

NHSE commissioning recommendations[16] advised that aseptic compounding services should be avoided to compound vial into a syringe, due to the ongoing constraint in capacity (commercial and NHS). Local services will need to consider how to take account of the need to draw up the drug rather than using a pre-filled syringe.

9. When does the Lucentis® PFS come off patent?

Lucentis® pre-filled syringe was due to come off patent mid-2023. This paves the way for ranibizumab biosimilar development in a pre-filled syringe providing a 'like for like' product.

The ranibizumab biosimilar Byooviz® 10mg/ml solution for injection vial (Samsung Bioepis)[17] was launched in the UK in 2023. It is available in a pack with the filter needle and injection needle required for intravitreal administration, however not all pack sizes may be marketed.

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