NHS Greater Manchester Integrated Care

Greater Manchester High-Cost Drugs Commissioning Pathway for Wet Age-related Macular Degeneration in Adults

Version 1.1

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Consulted by: Wet Age Related Macular Degeneration (wAMD) Treatment Pathway Development Group (see Section 12)

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1. Introduction

Age related macular degeneration (AMD) is a chronic progressive degenerative disease of the macula typically affecting people over the age of 50 years. The macula is the centre of the retina, responsible for high quality central vision.

There are two types of advanced forms of the disease, commonly called 'dry' and 'wet' AMD. Most people are affected by the dry (atrophic) form which is a slowly deteriorating condition with no treatment at present. The wet (neovascular) form presents acutely and needs both urgent and chronic treatment over years. If left untreated, the diagnosis is poor with significant visual loss occurring within two to three years.

Prevalence of wet AMD (wAMD) in the UK is predicted to rise by 59% from 2015 to 2035 (29% rise from 2015-2025) with prevalence in the population over 50 rising from 1.85% in 2015 to 2.36% in 2035.[1]

An ageing population and projected increasing prevalence of wAMD is associated with a significant cost burden to the NHS, as well as resource implications for existing AMD services, which is a cause for increasing concern.

2. Aims

Patients with late AMD (wet active) require timely and efficient treatment to prevent rapid decline in vision in the affected eye(s). This requires early diagnosis, prompt referral and protocol-based treatment to stabilise visual function.

The standard of care for wAMD is to treat with intravitreal injections of anti- VEGF (vascular endothelial growth factor) therapy, which targets the neovascularisation process and subsequent vascular leakage into the retina. These are high-cost drugs and represent some of the highest prescribing spend within secondary care, accounting for around £450 million NHS spend in 2015-2016.[2]

There is variation of anti-VEGF prescribing for wAMD across Greater Manchester (GM), with some localities adopting local treatment pathways. Clinician engagement

has also identified some variation in prescribing practice between ophthalmologists. This emphasises the need to standardise practice to enable an optimised approach to wAMD management, in order to:

- Maintain high quality, equitable standards of care
- Reduce unwarranted variation
- Maintain clinical choice
- Maintain patient choice
- Support use of NICE approved, licensed anti-VEGF therapies in line with marketing authorisation
- Provide safe, effective, evidence-based therapy
- Increase the use of more cost-effective therapies
- Make best use of NHS resources
- Re-invest savings to increase capacity of AMD services so that patients can be seen in a timely manner and with potential for earlier treatment

As new drugs including biosimilars and novel delivery systems emerge, there is potential to cultivate further variation in prescribing trends. This document aims to support the development of a harmonised GM wet AMD treatment pathway to optimise use of existing and new anti-VEGF therapies by evaluating:

- Clinical evidence
- Cost impact data
- National Commissioning Policy for medical retinal vascular medicines
- Local and national expert opinion
- Anti-VEGF prescribing/audit data
- Barriers to biosimilar implementation
- Resources required to support use of biosimilar
- Stock supply assurance

3. Clinical and Commissioning Guidance

The following clinical and commissioning guidance were in scope and used to develop this pathway:

3.1 NICE guidance

The following anti-VEGF agents are licensed for wet AMD and are recommended by NICE according to technology appraisal (TA) guidance:

- Aflibercept NICE TA294[3]
- Brolucizumab NICE TA672[4]
- Faricimab NICE TA800[5]
- Ranibizumab NICE TA155[6]

NICE[2] recommends offering intravitreal anti-VEGF treatment for late AMD (wet active) if all of the following circumstances apply in the eye to be treated:

- the best-corrected visual acuity is between 6/12 and 6/96
- there is no permanent structural damage to the central fovea
- the lesion size is less than or equal to 12 disc areas in greatest linear dimension
- there is evidence of recent presumed disease progression (blood vessel growth, as indicated by fluorescein angiography, or recent visual acuity changes)

AND

- the manufacturer provides drug with the discount agreed in the patient access scheme

There may also be situations where anti-VEGF treatment may be considered and NICE[2] makes the following recommendations:

- In eyes with visual acuity of 6/96 or worse, consider only if a benefit in the person's overall visual function is expected (for example, if the affected eye is the person's better-seeing eye).
- In eyes with visual acuity better than 6/12 anti-VEGF treatment is clinically effective and may be cost effective depending on the regimen used.

Some NG82 recommendations are outside of mandatory commissioning requirements.

This commissioning guidance does not make a recommendation for the off-label use of Bevacizumab[7] (Avastin®) for wAMD. However, given the NICE guideline committee's view that there is equivalent clinical effectiveness and safety of different anti-VEGF agents (aflibercept, bevacizumab and ranibizumab), comparable regimens will be more cost effective if the agent has lower net acquisition, administration, and monitoring costs. Refer to Section 6.1.

N.B 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 TA.

3.2 NHSE National commissioning recommendations: Updated July 2023

NHSE England (NHSE) commissioning recommendations following the national procurement for medical retinal vascular medicines[8] recognises that medical retinal vascular conditions account for some of the highest cost and volume treatments used within secondary care. The document outlines the best value treatment choices and, if implemented have the potential to generate financial savings which can be re-invested into ophthalmology services.

It makes a recommendation that for patients commencing treatment for Wet AMD, clinicians should consider ranibizumab biosimilar, where this is clinically appropriate and there is capacity to do so. NHSE recognise that there will be specific clinical considerations where ranibizumab biosimilar will not be clinically appropriate and support clinicians to consider alternative anti-VEGF therapies i.e. aflibercept, brolucizumab or faricimab.

3.3 Royal College Guidance: June 2021

Commissioning guidance from the Royal College of Ophthalmologists Age Related Macular Degeneration Services[9] highlights that whilst ranibizumab was the first licensed anti-VEGF treatment for wet AMD, many centres switched to using aflibercept as first-line therapy following NICE approval in 2013. This was due to aflibercept's treatment schedule (i.e. three initial loading doses followed by bimonthly treatment in the first year), providing the opportunity to reduce the need for monthly review appointments in comparison to ranibizumab (Lucentis®), with the potential to offer a more cost-effective treatment option.

At the time of publication of this guidance brolucizumab was new to the UK market and faricimab was not available. The commissioning guidance recognises that the choice of first-line agent will be guided by service set up, locally agreed costs, and local audit of treatment results.

4. Biosimilars

4.1 Understanding biological and biosimilar medicines

Biological medicines are large, complex molecules made or derived from a biological source. Examples of use include hormone therapies, insulin, vaccines, monoclonal antibodies and gene therapies.

Biosimilar medicines are a type of biological medicine which are highly similar in structure and function to an existing, approved biological medicine (i.e. 'reference' or 'originator' product). Biosimilar medicines have proven clinical equivalence and immunogenicity to the originator. Biosimilars have the potential to offer the NHS considerable cost savings.

4.2 Initiating treatment with a biosimilar

Biosimilar medicines are approved to be therapeutic equivalents to the reference medicine, as they must establish that they are just as safe and effective as the reference medicine. If demonstrated for one indication, safety and efficacy data may be extrapolated to other indications already approved for the reference medicine.

4.3 Anti-VEGF biosimilars

Ongavia® (Teva) was the first licensed ranibizumab biosimilar to be launched in the UK in 2022. Further ranibizumab biosimilars became available in 2023 i.e. Byooviz® (Biogen) and Ximluci® (Thornton & Ross). These biosimilars have the same licensed indications in adults as the reference product Lucentis®, so can be used in patients where Lucentis® would be a clinically suitable treatment option.

GMMMG provides guidance for the prescribing of high cost biosimilar biological medicines.[10]

5. Key considerations in GM wAMD treatment pathway development

This section outlines the process involved and specific considerations required in the development of a harmonised GM wAMD treatment pathway.

5.1 Clinician engagement

To ensure successful implementation of a GM wide wAMD treatment pathway, prescribing clinicians/ophthalmologists from hospital Trusts and independent service providers across GM have been consulted with. Expert opinion, real-world experience and audit data have been considered in the development of the treatment pathway. There has been an opportunity to discuss and address clinician concerns regarding safety, efficacy, and resource capacity.

Refer to Appendix 2: FAQ

5.2 Patient choice and consent

NHSE[8] acknowledges that the patient's needs and wishes should be taken into consideration when a prescribing decision is being made. Patient and/or carer consent is required, so it is important to engage and educate patients, with the provision of user friendly information resources, such as the SPS Ranibizumab biosimilar Patient Information Sheet[11] which can be adapted locally. Patient information should reflect national guidance and commissioning recommendations and provide a balanced viewpoint. Available resources can be adapted to reflect the requirements of the service.

Services will need to consider additional patient/appointment time required for counselling and consenting patients when switching treatments. When selecting the most appropriate treatment for an individual patient, the clinician may consider injection frequency and number of hospital visits if these are likely to cause significant distress or difficulties for the patient, with the potential to adversely impact treatment outcomes.

5.3 Safety and efficacy

The first line anti-VEGF treatment options i.e. aflibercept, faricimab and ranibizumab have demonstrated equivalent safety and efficacy, with no clinically significant differences.[12,23]

NICE NG82[2] compared aflibercept, bevacizumab and ranibizumab and stated that visual acuity outcomes were neither clinically nor statistically significantly different such that the 3 anti-VEGF agents can be considered equally effective.

The Appraisal Committee for NICE TA294[3] noted that aflibercept at its licensed dose was shown to be clinically non-inferior to ranibizumab in terms of visual acuity outcomes at 96 weeks. No statistically significant differences in visual outcomes between aflibercept and ranibizumab were reported.

Although there are no head-to-head trials for faricimab vs ranibizumab, evidence from two phase 3 randomised controlled trials[12] suggested that faricimab and aflibercept were similarly effective and had similar adverse events. This can be used to provide an indirect comparison for faricimab vs ranibizumab.

Brolucizumab demonstrated similar efficacy to aflibercept and ranibizumab, however there were additional safety concerns related to the risk of intraocular inflammation with short dosing intervals.

Phase III randomised clinical trials have demonstrated similar safety profile and immunogenicity of ranibizumab biosimilars to the reference product Lucentis®.[14,15,16]

All anti-VEGF preparations must be prescribed by brand to ensure that the patient receives the same product every time.

5.4 Cost effectiveness

The clinician should prescribe the most cost-effective anti-VEGF, that is clinically appropriate for the individual patient, taking into consideration:

- Biosimilar availability
- Administration costs
- Injection frequency
- Number of appointments required
- Monitoring requirements and associated costs
- Price per dose and commercial arrangements

This should be considered in the context of clinic capacity to deliver the specific anti-VEGF treatment, which may require additional clinic staff or longer appointment times.

To support commissioning recommendations[8], NHSE developed an Anti-VEGF resource impact calculator to demonstrate the cost impact and potential savings with different anti-VEGF prescribing scenarios for wAMD. This can support commissioners,

clinicians, and providers to inform prescribing decisions and influence change in prescribing practice.

Refer to Appendix 2: NHSE Resource impact calculator

5.5 Product formulation

Lucentis® (ranibizumab), Eylea® (aflibercept) and Beovu® (brolucizumab) are available as pre-filled syringes. Ongavia®, Byooviz® and Ximluci® are only available in a vial presentation and, require preparation prior to administration. This may require more clinic time to administer, and clinical staff may require additional training, if they have never used a vial before.

Refer to Appendix 2: FAQ for further information

5.6 Treatment strategies

Ranibizumab (Lucentis®, Ongavia®, Byooviz®, Ximluci®), aflibercept (Eylea®), brolucizumab (Beovu®) and faricimab (Vabysmo®) are all licensed for the following treatment strategies that are used within clinical practice:

- Treat-and-Extend (TREX)
- AS REQUIRED/NEEDED (PRN)
- Continuous or fixed dosing

TREX

A TREX dosing regimen can help reduce treatment burden by extending injection intervals, after initial loading phase when possible and achieves visual outcomes superior to as-needed treatment regimens. Furthermore, the 1-year results from a large randomised clinical trial[17] suggest that a TREX regimen is a viable and effective alternative to fixed monthly therapy in treatment-naive wAMD patients.
TREX is being adopted in clinical practice as it represents a patient-centric and economical option.

PRN

UK retina specialists reported[17] on best practice recommendations in wet AMD management in clinical practice. PRN protocols used in clinical trial settings may not

accurately reflect actual treatment patterns with PRN regimens in routine practice, which can follow less stringent retreatment criteria and variable or indeterminate monitoring. As such, a PRN retreatment regimen often tends to lead to undertreatment with an insufficient frequency of anti-VEGF injections, resulting in poorer vision outcomes than those observed in pivotal nAMD randomised controlled trials.[19,20,21,22]

Continuous dosing

Registration studies such as ANCHOR/MARINA[22] and VIEW 1/2[23] demonstrated the effectiveness of ranibizumab and aflibercept, respectively, when administered continuously at fixed frequent intervals. However, given the treatment burden and cost with monthly or bimonthly fixed-interval treatment, there has been great interest in alternative dosing regimens.

5.7 Injection frequency

The dosing strategy employed will determine injection frequency and dosing intervals.[25] A key aim in anti-VEGF treatment has been to reduce the frequency of injections required, whilst maximising visual acuity outcomes and preventing disease progression. This supports a personalised approach and allows the clinician to individualise treatment for the particular patient.

All treatment appointments occur in an outpatient clinic as a 'one-stop' model, where monitoring and treatment occur at the same time. In people with bilateral late AMD (wet active), both eyes are usually treated at the same appointment.

5.8 Monitoring

Monitoring occurs in the 'one-stop' clinic appointment:

- Monitoring is performed by an OCT examination. At baseline, confirmation of macular neovascularisation is advisable using OCT angiography or fluorescein angiography
- An OCT is performed at every treatment appointment.
- Additional monitoring visits are required for patients receiving PRN and TREX treatment, because these regimens will involve some appointments at which the clinician decides that treatment is not needed.

5.9 Off label use

Bevacizumab

Bevacizumab (Avastin®) currently only has a UK market authorisation for non-ophthalmology indications. If used for wet AMD it will be considered as 'off-label' use by the Medicines and Healthcare products Regulatory Agency (MHRA) and requires pre-requisites to be met.[33] This needs to be considered when deciding to prescribe bevacizumab.

Although bevacizumab has shown comparable safety and efficacy to ranibizumab and aflibercept, its current unlicensed status for wet AMD has precluded its inclusion in the wet AMD treatment pathway. This may change with the emergence of new products e.g., an investigational ophthalmic formulation of bevacizumab is under development.

Anti-VEGF injection clinics led by nurses and other AHPs

Use of non-medical staff for injection administration remains off-label for ranibizumab and brolucizumab. However due to significant capacity and workload issues ophthalmology clinics have utilised trained nurses and other allied healthcare professionals (AHPs) to administer intravitreal injections. Ophthalmic nurse practitioners, hospital optometrists, technicians and orthoptists play an increasingly significant role in the delivery of routine retina care, with extended roles helping to expand service provision capacity. A positive patient satisfaction response with a nurse-led injection service has been demonstrated, comparable to a doctor-led service, and with an acceptable safety profile.[18]

Note: Faricimab and Aflibercept are licensed to be administered by a 'qualified healthcare professional' experienced or trained in intravitreal injections.

Refer to Appendix 2: FAQ

Treatment intervals

Due to the increasing use of PRN and TREX treatment posology extension of treatment intervals outside of product licensing is seen in routine clinical practice. A UK expert panel[25] provided recommendations for an aflibercept TREX pathway, to a maximum treatment interval of 16 weeks extended in 2 to 4 weekly increments. Faricimab has a licensed treatment interval of up to 16 weeks.

This is considered within the context of service capacity.

5.10 Service capacity

Successful implementation of biosimilar medicines in the treatment pathway requires careful planning and consideration of:

- Identification of suitable patient cohort
- Clinic capacity
- Adequate staffing
- Staff competency and training
- Operational impact
- Pharmacy provision i.e., procurement, stock management

5.11 Endophthalmitis risk

Endophthalmitis is an Infection that involves the internal structures of the eye. It usually poses a serious threat to the visual function of the eye and is a rare complication of intravitreal injection.

The risk of endophthalmitis after anti-VEGF therapy is approximately 0.02-0.09% from randomised controlled trial data whereas real-world evidence from large cohorts suggests 0.028%.[26] The cumulative risk per individual increases with increasing number of injections. A number of prophylactic strategies are employed to reduce the rate of post-intravitreal endophthalmitis, such as use of topical Povidone Iodine 5% pre-injection and strict adherence to aseptic protocols.

A retrospective study[28] compared the risk for post-injection endophthalmitis between different anti-VEGF agents and syringe preparation techniques. The results demonstrated that the endophthalmitis risk following injections with syringes that were prefilled by GMP pharmacies or the manufacturers was significantly lower than that following injections which were self-drawn by the physician (0.019% vs. 0.055%, $p < 0.0001$). For ranibizumab, risk of endophthalmitis decreased since it became available in a prefilled syringe (0.054% vs. 0.014%, $p = 0.066$), bordering on statistical significance.

In a large, multicenter, retrospective cohort study[28] the use of prefilled syringes vs conventional preparation during intravitreal injection of ranibizumab was associated

with a reduced rate of culture-positive endophthalmitis. In the conventional ranibizumab group, a total of 43 cases of suspected endophthalmitis occurred (0.026%; 1 in 3845 injections) and 22 cases of culture-positive endophthalmitis occurred (0.013%; 1 in 7516 injections). In the prefilled ranibizumab group, 12 cases of suspected endophthalmitis occurred (0.015%; 1 in 6534 injections) and 2 cases of culture-positive endophthalmitis occurred (0.0026%; 1 in 39 204 injections).

Results from the 48-week randomised trial COLUMBUS-AMD[14] comparing safety and efficacy of biosimilar Ongavia vs reference product Lucentis reported 1 patient in the reference group (n=239) with severe endophthalmitis.

6. GM wet AMD anti-VEGF Treatment Pathway

Anti-VEGF therapy should be initiated in accordance with the criteria specified in the relevant NICE TA.

All licensed, NICE approved anti-VEGF therapies may be considered as treatment options; however, the **preferred** option (see 6.1) should be the lowest cost treatment (taking account of drug, administration, and monitoring costs) that is clinically appropriate. The commissioning recommendations are not intended to restrict clinical judgement when determining the most appropriate treatment for an individual. Treatment choice should be considered within the context of the specific needs of the patient and the capacity of the service to deliver the prescribed treatment.

Local treatment pathways may define specific clinical characteristics where one anti-VEGF may be favoured over another. There should be a clear rationale, with supporting evidence for prescribing decision.

6.1 First line Options (including sequential use):

Ranibizumab biosimilar

Ranibizumab (Lucentis®) was the first licensed anti-VEGF for treatment of wAMD, approved by NICE in 2008. There is considerable experience of use and extensive clinical evidence to support its use.

In new patients where ranibizumab is considered a clinically suitable option then the biosimilar should be prescribed, as this represents the **best value product**. The originator product Lucentis® should not be initiated for new patients and patients currently prescribed Lucentis® should be assessed and switched to ranibizumab biosimilar.

Aflibercept

Aflibercept was approved by NICE in 2013 and demonstrated that at its licensed dose was clinically non-inferior to ranibizumab in terms of visual acuity outcomes, and with a comparable safety profile.

However, the NICE Appraisal Committee[3] acknowledged the view from clinical specialists that an important advantage of aflibercept is that it requires less frequent administration than ranibizumab while achieving similar clinical outcomes, as seen in the clinical trials, thus imposing less burden on NHS capacity.

Aflibercept is currently the most widely used anti-VEGF for wet AMD across GM but may not offer the most cost-effective option in comparison to ranibizumb (biosimilar), even with the potential for extended treatment posology it offers.

Faricimab

Faricimab is a first-in-class dual-pathway inhibitor of Ang-2 and VEGF and was approved by NICE for wAMD in 2022. The NICE TA[5] recommends that if patients and their clinicians consider faricimab to be one of a range of suitable treatments (including aflibercept and ranibizumab), choose the least expensive treatment. Take account of administration costs, dosage, price per dose and commercial arrangements.

Faricimab is emerging as an appealing option for clinicians due to its licensed treatment posology and potential to extend treatment interval to a maximum of 16 weeks. Clinical studies[12] of faricimab have shown that at Week 48, 78.7% of patients in the faricimab dosing arm were on a dosing regimen of 12 weeks or longer. Overall, 21.2%, 33.4%, and 45.3% of patients were on an 8-weekly, 12-weekly, and 16-weekly dosing regimen respectively at Week 48, with non-inferior mean change from baseline BCVA when compared to aflibercept 8-weekly. Real world efficacy and safety evidence is emerging.[29]

6.2 Second line Option:

Brolucizumab (Beovu®)

Brolucizumab was approved by NICE in 2021. Clinical trial evidence showed that brolucizumab was similarly effective to ranibizumab and aflibercept.[4] Although generally well tolerated there are specific safety concerns with risk of intraocular inflammation and retinal vascular occlusion with short dosing intervals (i.e. 4 weekly during maintenance phase. MHRA[30] advised that to reduce the risk of these events after the maintenance dose, brolucizumab should not be administered at intervals of less than 8 weeks apart. Due to the risk profile of brolucizumab this is not routinely recommended as a first-line treatment option, without consideration of specific risk factors.[32]

A potential benefit of brolucizumab, demonstrated from clinical trials[31] is that greater than 50% of patients were maintained on a 12 weekly dosing interval following the loading phase.

6.3 Horizon scanning

As more biologics or reference products come 'off patent' there will be an emergence of more cost-effective biosimilars and new formulations. These are currently at various stages of development and expected to be launched in the UK over the next few years e.g., the first aflibercept biosimilar is expected in 2025.

Horizon scanning will identify new medicines in the pipeline and inform processes for managed entry of new products. Any new anti-VEGF therapies approved by GMMMG will be considered for inclusion in the wAMD treatment pathway, in accordance with the associated NICE TA.

7. Monitoring treatment

7.1 Monitoring disease activity

Response to anti-VEGF therapy is assessed at recommended intervals (in line with product SmPC and determined by prescribing clinician), using following:

- Visual acuity (VA) measurement using logMAR chart (from baseline)
- Macular morphology with optical coherence tomography (OCT) for both eyes
- Need for further tests or investigations will be determined by treating clinician

7.2 Stable disease

Stable disease is defined clinically as 2-3 visits at maximal extension based on posology of the drug used (12 or 16 weeks) with dry retina and stable VA. However, this is subject to clinician discretion and varies with individual patient.[9]

If the disease appears stable, observation without giving anti-VEGF treatment may be considered. Risk stratification and effective triage are necessary to identify suitable patients. These patients may be referred to an optometrist or nurse-led stable AMD clinic, according to local policy and availability of this service.[18]

Some patients may be suitable candidates for self-monitoring with the use of appropriate strategies and monitoring techniques. This will be complementary to standard clinical assessment.

If at any time there is presence of disease activity treatment and monitoring intervals should be resumed at clinician's decision.

7.3 Treatment failure

For patients who have a suboptimal response, or 'non-responders' should be clinically assessed for need for further diagnostic investigations, to consider differential diagnosis i.e., idiopathic polypoidal choroidopathy or central serous chorioretinopathy.

Clinicians should consider either stopping treatment or changing to an alternative anti-VEGF. Ensure that patients are actively involved in all decisions about the stopping or switching of treatment.

8. Switching treatment

8.1 Changing from 'reference' to biosimilar product

Considerations when switching to a biosimilar:

- Decision to switch should be part of a shared decision between the patient and/or carer and prescribing clinician, with an explanation for the reason for changing

- Patients should be assured that the biosimilar is comparable to the original product in terms of quality, safety, and effectiveness
- The switch should be done at the point of prescribing and not at the point of dispensing or administration
- The biosimilar should be prescribed by brand to ensure that patients prescribed biologic or biosimilar can be identified
- A patient leaflet should be provided to the patient providing information about the biosimilar
- Determine if any additional local monitoring is required after switch

8.2 Sequential use

Switching to another anti-VEGF agent may be considered in the following circumstances:

- **Non-response** to therapy, despite treatment with an optimally delivered treatment regimen. It has been suggested that drug tolerance may play a role in a subset of anti-VEGF refractory patients (persistent fluid on OCT despite monthly injections for ≥6 months) who benefit from a treatment switch.[36]
- **Allergy** or **hypersensitivity**
- **Adherence** e.g. switch to a fixed regimen rather than TREX protocol to aid adherence to treatment

NHSE recommends that if initial treatment selected was ranibizumab biosimilar, clinicians should consider changing to aflibercept, brolucizumab or faricimab.

9. Discontinuing treatment

NICE[2] recommends that treatment be continued only in people who maintain an adequate response to therapy. Criteria for permanent discontinuation should include persistent deterioration in visual acuity and the identification of anatomical changes in the retina that indicate an inadequate response to therapy despite an optimally delivered treatment regimen. Treatment with an anti-VEGF should be stopped if the eye develops late AMD (wet inactive) with no prospect of functional improvement or hypersensitivity to an anti-VEGF.

Clinicians may consider temporarily withholding treatment if there is no disease activity (i.e. disease has become inactive at ~6 to 12 months), stable disease activity despite frequent and timely dosing and early review (i.e. at 2 weeks to confirm a lack of further response), or there has been one or more adverse events related to drug or injection procedure. If there is recurrence of neovascularisation, treatment is reinstated until lesion stabilisation is achieved, as indicated by best corrected visual acuity and/or lesion morphology.

Refer to key expert opinion for further guidance.[17,36]

10. Commissioning considerations

To be determined.

10.1 Biosimilar implementation

NHSE have confirmed that the on-boarding process has now been removed with the availability of 3 ranibizumab biosimilars (Byooviz, Ongavia, Ximluci). Provider Trusts can order stocks from dedicated wholesalers via their usual route. Manufacturers have provided a commitment to maintaining a supply of biosimilar product.

11. Data requirements and audit

11.1 Monitoring

It is important to establish robust processes for data collection and analysis to support providers and commissioners to monitor compliance with commissioned pathways and monitor impact on patient outcomes.

Due to the risks of permanent loss of vision in retinal conditions treated by intravitreal injections, it is crucial that clinicians work with commissioners and Trust Leads to ensure appropriate regular quality and safety monitoring reported using agreed data sets and Key Performance Indicators (KPIs). This may include KPI targets for: Number of new referrals clinically suitable for treatment; Time from referral to first injection; Number of new patients initiated on biosimilar; Number of new patients initiated on

aflibercept; Number of new patients initiated on faricimab; Number/percentage of patients switched from originator to biosimilar; Average number of injections in Y1/Y2/Y3; Completion of BlueTeq® forms.

Significant safety events must be reported via the local incident reporting system so that these can be captured both locally and nationally via the National Reporting Learning System (NRLS).

For new drugs, MHRA encourages the reporting of **ALL** suspected reactions via the Black Triangle Scheme (https://www.gov.uk/drug-safety-update/the-black-trianglescheme-or) as part of post-marketing surveillance.

11.2 Audit

The Royal College of Ophthalmologists are conducting an audit[39] for Wet AMD which supports improvement in quality of care which is an important quality assurance measure. Further information can be found at: AMD Audit Clinical Data Set.pdf (nodaudit.org.uk). All units are encouraged to actively contribute to the Royal College of Ophthalmologist National Ophthalmology Database dataset.

11.3 Blueteq®

Where Blueteq has been introduced to the trust as part of the contractual arrangements, funding approval for the Payment by Results (PbR) excluded high cost drugs will be made by meeting the accepted criteria outlined on completion and submission of a Blueteq form.

12. Wet AMD Treatment Pathway Development Group

A sub group of the GM wet AMD Working Group was formed to advise on the development of the GM wet AMD Commissioning Pathway:

Name	Designation	Organisation
Humera Ahmed (Chair)	Senior Medicines Optimisation Adviser	Manchester Integrated Care Partnership
Kenny Li	Chief Pharmacist	NHS Greater Manchester Integrated Care
Lara Shah	Deputy Head of Medicines Optimisation (Strategy)	Manchester Integrated Care Partnership
Sajjad Mahmood	Consultant Ophthalmic Surgeon Clinical Lead, Medical Retina	Optegra Eye Heath Care
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Shakti Thakur	Consultant Ophthalmologist	Bolton NHS Foundation Trust
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Susan Parker	Eye Care Clinical Advisor	NHS Greater Manchester Integrated Care (Stockport)
Leigh Lord	Head of Medicines Optimisation and Governance	Manchester University NHS Foundation Trust (MFT)
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Hafsa Sattar	Lead Pharmacist, High Cost Drugs, Homecare and Third Party Business Solutions	Bury & Rochdale Care Organisation (Northern Care Alliance NHS)
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- Mr Robin Hamilton Consultant Ophthalmologist, Moorfields Eye Hospital
- Mrs Melanie Hingorani Consultant Ophthalmologist, Moorfields Eye Hospital
- Shu Yi Tan Contracting and Commissioning Pharmacist, NHS London Shared Service
- See Mun Wong Interim Pharmaceutical Market Support Group (PMSG) Lead North West
- Mary-Jo Pryor Strategic Category Lead, Commercial Medicines Directorate NHSE/I

13. Glossary

Abbreviation	Description
BCVA	Best Corrected Visual Acuity
CNV	Choroidal Neovascularisation
DMO	Diabetic Macular Oedema
IVT	Intravitreal
Myopic CNV	Myopic Choroidal Neovascularisation
nAMD	neovascular Age-related Macular Degeneration
OCT	Optical Coherence Tomography
PDR	Proliferative Diabetic Retinopathy
PDT	Photodynamic Therapy
RCOphth	The Royal College of Ophthalmologists
RVO	Retinal Vein Occlusion
VA	Visual Acuity
VEGF	Vascular Endothelial Growth Factor
wAMD	Wet Age-Related Macular Degeneration

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