NHS
North East London

High cost drugs treatment pathway for wet age-related macular degeneration

NHS North East London

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Authors and contributors	**NHS NEL** Commissioning and Contracting Pharmacist Commissioning and Contracting Senior Pharmacy Technician **Barts Health NHS Trust:** Consultant Ophthalmologist Surgery and Critical Care Pharmacist **Barking, Havering and Redbridge University Hospitals NHS Trust:** Consultant Ophthalmologist Lead Pharmacist, Surgery and Gastroenterology Clinical Surgical Pharmacist
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25/11/2025	1.0	New document

Contents

1. Scope

This document outlines the high cost drugs treatment pathway for adult patients in north east London diagnosed with wet age-related macular degeneration (wet AMD). This treatment pathway offers a best value approach as a whole and outlines criteria that enable switching if patients don't respond fully to treatment or if they don't reach the expected dosing interval within a specific time interval.

The pathway underpins guidance from NHS England (NHSE) and has been developed in collaboration with ophthalmologists and specialist pharmacists in NEL acute provider trusts. It is to be used in conjunction with the National Institute for Health and Care Excellence (NICE) guidance and the published NICE technology appraisal (TA) guidance for each individual biologic therapy. The pathway is intended to be adopted by all acute provider trusts within north east London.

2. NHSE guidance

At the time of publication, this treatment pathway considers the following NHSE commissioning guidance: medical retinal treatment pathway in wet age-related macular degeneration (version 1.3, last updated October 2025, accessed via NHS Futures).

3. NICE guidance and technology appraisals

At the time of publication, this treatment pathway considers the following NHSE guidance: NICE NG82 Age-related macular degeneration (23/01/2018)

Table 1: NICE technology appraisals for wet age-related macular degeneration

At the time of publication, this treatment pathway considers the following NICE TAs.

NICE TA number	Date published/ updated	Title
TA155	Updated 20/05/2024	Ranibizumab and pegaptanib for the treatment of age-related macular degeneration
TA294	24/07/2013	Aflibercept solution for injection for treating wet age-related macular degeneration
TA800	29/06/2022	Faricimab for treating wet age-related macular degeneration
TA1022	04/12/2024	Bevacizumab gamma for treating wet age-related macular degeneration
TA672	03/02/2021	Brolucizumab for treating wet age-related macular degeneration

4. Principles

This document is based on current NICE TAs and NHSE commissioning guidance: medical retinal treatment pathway in wet age-related macular degeneration. The document also reflects local agreements which are based on clinical evidence considered by the NEL ophthalmology working group. The prescribing pathway has taken into consideration the Regional Medicines Optimisation

Committee (RMOC) Advisory statement on the sequential use of biologic medicines (updated 07/05/2020) to formulate a position which meets the needs of patients in the region.

Local agreements outside of NICE recommendations aim to address unmet clinical needs, and the use of medicines outside of NICE TAs will be monitored on a regular basis through Blueteq or clinical audit where Blueteq is not used.

The pathway is subject to change as new evidence, NICE TAs or local agreements are released or updated that will impact on the information outlined in this document. This includes changes in drug costs that may impact on cost effectiveness and drug choice in the treatment pathway.

It is expected that drugs presenting best value are selected where clinically appropriate.

For further prescribing information including contraindications and cautions, please refer to the relevant drug monograph in the latest version of the British National Formulary (BNF) or the respective drug's Summary of Product Characteristics (SPC).

5. Eligibility criteria

The following vascular endothelial growth factor inhibitors (anti-VEGFs) are considered in the NEL wet AMD treatment pathway: aflibercept, ranibizumab, faricimab, bevacizumab gamma and brolucizumab. In line with NICE recommendations, wet AMD patients are eligible for intravitreal anti-VEGF treatment where all of the following criteria are met:

- The eye has a best-corrected visual acuity (BCVA) between 6/12 and 6/96
- There is no permanent structural damage to the central fovea
- The lesion size is 12 disc areas or less in greatest linear dimension
- There are signs of recent disease progression (for example, blood vessel growth as shown by fluorescein angiography, or recent visual acuity changes)

NICE NG82 (not mandatory) recognises the use of anti-VEGFs outside visual acuity criteria set in NICE TAs, depending on the drug and regimen used. **This recommendation has not been agreed within NEL ICS and is therefore not applicable to this pathway.**

6. Choice of therapy

The choice of treatment should be made after discussion between the clinician and the patient about the advantages and disadvantages of the treatments available. This may include consideration of the patient's medical history, injection burden, harmonisation of treatment for both eyes, previous non-responder or side effects/sensitivity reactions to a previous anti-VEGF in the other eye.

The RAG (red, amber, green) system has been implemented as a means of communicating the differences in cost between treatment options.

- **First choice (green)** – where clinically appropriate, use **aflibercept 2mg (switch to biosimilar once available)** and **ranibizumab biosimilar** as first choice options. These are the most cost effective options, (taking into account administration costs, frequency and drug cost per annum) according to NHSE modelling based on real world data and projected biosimilar savings.
- **Second choice (amber)** – **aflibercept 8mg (preferred)** and faricimab as second choice options. This is usually when high injection frequency is not acceptable with first choice options in the following cohort of patients:

    - Learning difficulties
    - Dementia
    - Requiring hospital transport
    - Requiring treatment in the operating theatre under sedation/ deep sedation/ general anaesthesia
    - Co-morbidities requiring hospital appointments/ inpatient admissions (e.g. chemotherapy)
- **Third choice (red)** – brolucizumab and bevacizumab gamma (licensed) are recommended as third choice options. Bevacizumab gamma is the least cost effective option and there is higher rate of severe intraocular inflammation with brolucizumab.

Treatment harmonisation

Where one eye is already on treatment, but the other eye qualifies for another treatment, prioritise treatment harmonisation by choosing the best treatment options for both eyes (i.e. using only one drug for both eyes). This strategy minimises drug administration error and allows easy identification of adverse drug reactions of a single drug compared to administering two different drugs.

Capacity constraints

Capacity constraints are normally represented by inability within a service to deliver treatment in a timely way to patients as part of business as usual. Provider trusts are robustly encouraged to transform their services to create the capacity which their service demands, using some of the savings generated by first choice agents.

7. Treatment regimen

Treat and extend

A treat and extend regimen based on BCVA and optical coherence tomography (OCT) is recommended. The interval for the next anti-VEGF injection is extended by 2 to 4 weeks at clinician's discretion, up to a maximum of 12 to 20 weeks based on disease activity and the licensed dosing intervals – see appendix 3.

Treatment pause

Clinicians may consider temporarily withholding treatment if there is no disease activity (i.e. disease has become inactive on maximum extension after 2 to 3 doses) – see appendix 3. If there is recurrence of disease activity, **treatment can be reinstated** until disease stabilisation is achieved, as indicated by BCVA and/or lesion morphology.

8. Switching treatment

Consideration for treatment switch

- Suboptimal response after loading phase or (post-loading) at any other point due to resistance to current agent after 3 consecutive monthly intravitreal injections AND

there is still potential for improvement in vision, or improved stabilisation at 6/96 or better, with further treatment.
- Symptoms of allergy or presumed tachyphylaxis.
- Adverse events related to drug.
- Frequent injections (e.g. < 8-week intervals) required to maintain disease stability and treatment burden not acceptable to either patient or service delivery
- When patient injection burden is highlighted
- Where treatment harmonisation is required (see above)

Switching between anti-VEGF treatments

- If the patient failed at least two extended interval attempts and there is no clinical benefit:
    - Switch back to the previous anti-VEGF if it is more cost-effective and clinically appropriate.
    - Consider switching to an alternative anti-VEGF if this is the patient's second anti-VEGF.
- A maximum of **THREE lines of therapy** will be commissioned per eye, with the expectation that the first anti-VEGF used should normally be first choice options.
- When switching to a different anti-VEGF, it would be a clinical decision to determine whether reloading is required.

9. Assessment of response and stopping treatment

For most patients, the main treatment goals are:

- Preservation of visual function (e.g. BCVA improvement or stabilisation)
- Anatomical improvement from OCT (e.g. lesion size, fluid in retina, haemorrhage) with no signs of disease activity

The management of the patient should be reviewed by a senior specialist annually to consider if continuation of treatment is in the patient's best interest. After 12 months of intravitreal injections, most patients are expected to have:

- Stabilisation of visual function (improvement or preservation)
- Anatomical improvement from OCT (e.g., lesion size, fluid in retina, haemorrhage). Note that changes in OCT precedes visual function tests.

Some patients will have stable disease activity or persistent subretinal fluid despite frequent and timely dosing. This is due to the progressive nature of wet AMD. Consider early review (i.e. at 2 weeks to confirm a lack of further response). In addition, responses can be affected by other causes and may require further assessments to confirm a true suboptimal or poor response. Examples include, but not limited to:

- Not consistently wearing vision correction equipment at each visual assessment
- In early dementia patients where comprehension may fluctuate at each visit
- Development of cataracts

Review with consideration to stop treatment if:

- Visual acuity < 25 letters (absolute) on 2 consecutive visits despite optimum treatment AND
- Attributable to wet AMD in the absence of other pathology AND
- Structural results (e.g. OCT) suggest no prospect of visual improvement with continued treatment.

When reviewing the patient, consideration should be given to whether they may benefit from switching to another anti-VEGF or if they are unlikely to benefit from further anti-VEGF therapy. In the latter case, treatment should be discontinued permanently. **Discontinue treatment permanently if yes to all the below):**

- Has the patient completed loading phase?
- Is the patient's treatment optimised (i.e. they have been receiving adequate injections at optimal intervals on time)? *On average, a patient initiated on treatment would require 6 injections in the first year and 5 injections in the second year. From the third year, an average of 5 injections are required to prevent decrease in vision due to inadequate treatment.*
- Has the patient exhausted a reasonable number of treatment options (maximum of THREE lines of anti-VEGFs are recommended)?
- Is the treated eye the WORSE seeing eye?
- Does the patient agree that they DO NOT receive continuing benefits from treatment?

Permanent discontinuation of anti-VEGF treatment recommended if:

- Visual acuity < 15 letters (absolute) on 2 consecutive visits despite optimum treatment AND
- Attributable to wet AMD in the absence of other pathology

Cataracts

If a patient is scheduled for a cataract operation within the next 3 months and if it is anticipated that vision will improve due to the procedure, the above discontinuation criteria may no longer apply, and patient may continue treatment and be reassessed following their cataract operation.

A decision support tool for wet AMD has been developed to support shared decision-making discussions with patients and is available here: https://www.england.nhs.uk/publication/decision-support-tool-making-a-decision-about-wet-age-related-macular-degeneration/

10. Lines of therapy

Only THREE lines of therapy will be commissioned per eye by the ICB under this pathway. The following scenarios should not count as a line of therapy:

- Switch from branded to biosimilar and vice versa, biosimilar to biosimilar switches for the same agent.
- Switch back to a previous anti-VEGF (i.e. those who did not experience clinical benefit after failed extended interval attempts with newer agents).
- Switch due to adverse drug events or allergy.

Worked examples

One line of therapy:

- Patient switched from branded drug A to biosimilar drug A
- Patient switched from drug A to B due to adverse drug events

Two lines of therapy:

- Patient had suboptimal response to drug A, now on drug B
- Patient had suboptimal response to drug A, switched to drug B and had a good clinical response. Unable to extend dose intervals beyond 7 weeks so switched to drug C. Still unable to extend dose intervals on drug C and no clinical benefit, so switch back to drug B because it is more cost-effective.

Three lines of therapy:

- Patient who had suboptimal responses to drugs A and B, now on drug C
- Patient had suboptimal response to drug A, then switched to drug B. Unable to extend dose intervals beyond 7 weeks on drug B so switched to drug C. Remains on drug C because has added clinical benefit compared to drug B even though unable to extend dose intervals further.

Adverse drug reactions

An adverse drug reaction to a medicine will not count as a line of therapy. However, the patient must have shown a response to therapy for that biologic after the initial response assessment period for it not to count as a line of therapy.

- If the patient has the adverse event **before** this assessment period, it will not count as a line of therapy.
- If the adverse reaction occurs **after** the initial response assessment period and the patient has shown a response to therapy with that biologic, it will not count as a line of therapy.

11. Funding

To support data-driven care, commissioners will be extracting outcomes data from Blueteq. In accordance with the pathway, Blueteq must be used for the management of all funding requests for anti-VEGF therapies. This includes recording treatment switches and cessation as a result of clinical review and/or remission, drug and formulation switching.

Provider trusts are expected to obtain funding via Blueteq both prior to initiation and for continuation of anti-VEGF treatments for wet AMD patients as described on the Blueteq forms.

Where Blueteq is not available, provider trusts are expected to have a governance process in place to ensure compliance to this pathway. Commissioners may request evidence to demonstrate compliance if necessary.

Patients transferred from out of area or from overseas

For patients who have already commenced on their treatment for wet AMD:

- If the current treatment is covered by a NICE TA, then the patient can continue their treatment as per the TA.
- If the treatment is not covered by a NICE TA, or this pathway, then an individual funding request (IFR) must be submitted to continue the funding for therapy.

Communication between healthcare providers

It is the responsibility of the Consultant Ophthalmologist to ensure the patient's GP is informed that the patient is receiving treatment with an anti-VEGF. It will then be the responsibility of the GP to update a patient's medical record with this medication.

12. References

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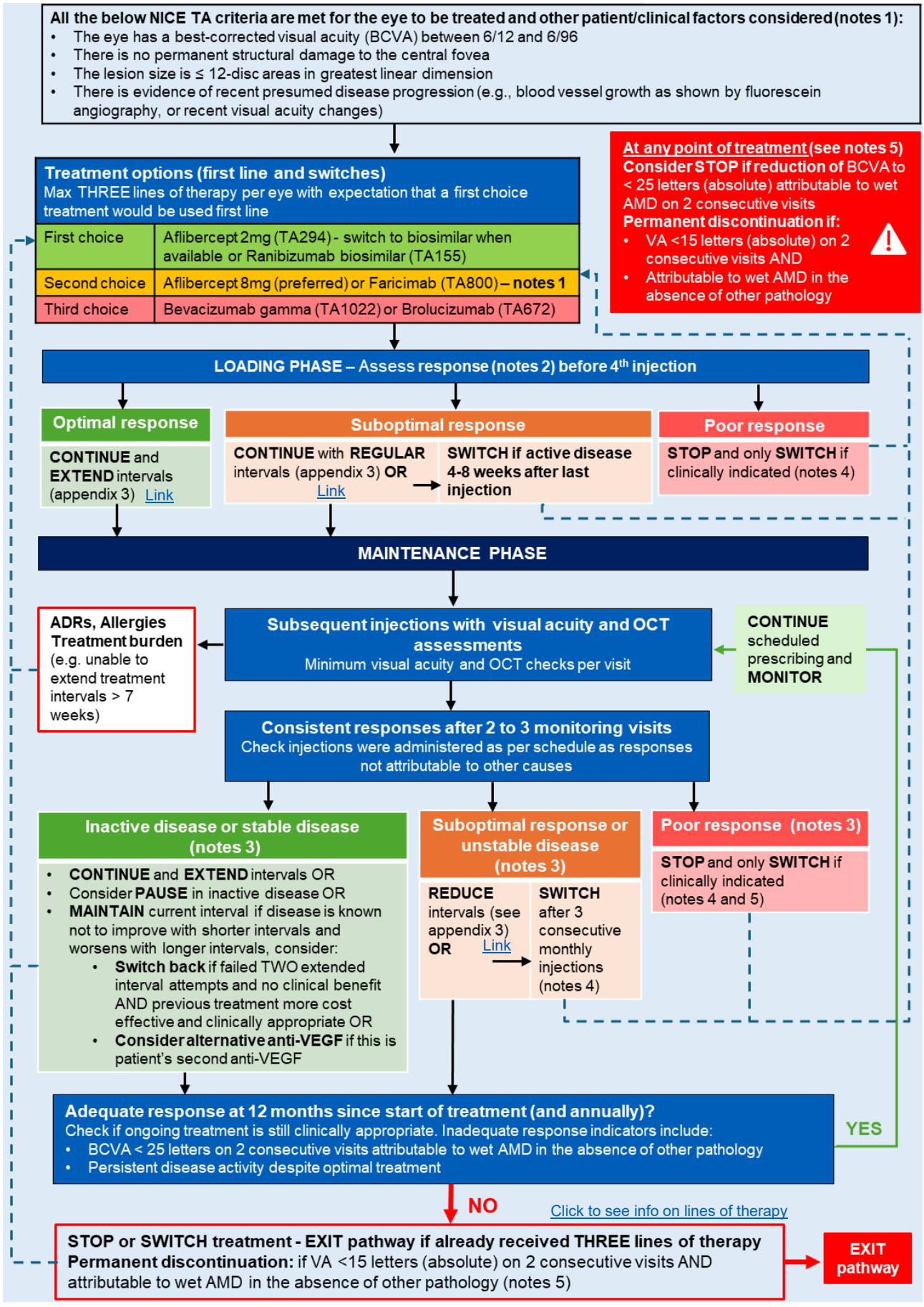
Appendix 1. Treatment algorithm for adult patients with wet age-related macular degeneration (wet AMD)

Click here for link to notes



Appendix 2. wet AMD pathway (notes)

Notes 1 - Treatment considerations (clinician's decision based on patient and clinical factors)
- **Previous non-responder** to ranibizumab/aflibercept in fellow eye
- **Ranibizumab-specific contraindications:** subretinal bleed >50% of lesion, idiopathic polypoidal choroidal vasculopathy
- **Brolucizumab:** higher rate of severe intraocular inflammation
- **Treatment harmonisation** - if one eye is already being treated and the other qualifies for a different treatment, prioritise harmonising treatment by using a single drug for both eyes. This reduces the risk of administration errors and simplifies monitoring for adverse drug reactions

Aflibercept 8mg (preferred) or faricimab may be used first line when high injection frequency is not acceptable with first choice options if patient has one of the below:
- Learning difficulties, dementia or requiring hospital transport
- Requiring treatment in the operating theatre under sedation/deep sedation/general anaesthesia
- Co-morbidities requiring frequent hospital appointments/inpatient admissions (e.g. chemotherapy)

Notes 2 – Treatment response post-loading
- **Optimal response -** BCVA improvement or stabilisation AND no disease activity on OCT
- **Sub-optimal response -** Improvement in disease activity on OCT but with signs of active disease e.g., fluid in retina, new haemorrhage, new subretinal hyper-reflective material (SRHM)
- **Poor Response -** BCVA < 25 letters (absolute) attributable to wet AMD on 2 consecutive visits
- **Permanent discontinuation:** if VA <15 letters (absolute) on 2 consecutive visits AND attributable to wet AMD in the absence of other pathology

Notes 3 – Treatment response during maintenance phase
Inactive disease or stable disease
- **BCVA:** improvement or stabilisation AND
- **OCT:** anatomical improvement or stabilisation (e.g., lesion size, fluid in retina, haemorrhage) OR no disease activity

Suboptimal response or unstable disease
- **BCVA:** worsens/no improvement (≤ 5-letter improvement) OR
- Improvement in anatomical features but signs of persistent activity.
- **OCT:** anatomical features of persistent active disease (e.g., non resolving fluid in retina, new haemorrhage or SRHM)
- **Poor Response -** BCVA < 25 letters (absolute) attributable to wet AMD on 2 consecutive visits
- **Permanent discontinuation:** if VA <15 letters (absolute) on 2 consecutive visits AND attributable to wet AMD in the absence of other pathology

Notes 4 – Switching considerations
- ADRs, allergy or presumed tachyphylaxis
- Frequent injections (e.g. < 8-week intervals) required to maintain disease stability and treatment burden not acceptable to either patient or service delivery OR when patient injection burden is highlighted
- Treatment harmonisation required
- Suboptimal response after loading phase or (post-loading) at any other point due to resistance to current agent after 3 consecutive monthly intravitreal injections AND there is still potential for improvement in vision, or improved stabilisation at 6/96 or better, with further treatment

When reviewing the patient, consideration should be given to whether they may benefit from switching to another anti-VEGF or if they are unlikely to benefit from further anti-VEGF therapy. In the latter case, treatment should be discontinued permanently.

Notes 5 – Stopping Treatment
REVIEW with consideration to stop treatment if:
- Visual acuity < 25 letters (absolute) on 2 consecutive visits despite optimum treatment AND
- Attributable to wet AMD in the absence of other pathology AND
- Structural results (e.g. OCT) suggest no prospect of visual improvement with continued treatment

Discontinue treatment permanently if yes to all the below:
- Has the patient completed loading phase?
- Is the patient's treatment optimised (i.e. they have been receiving adequate injections at optimal intervals on time)?
- Has the patient exhausted a reasonable number of treatment options (max 3 lines of anti-VEGFs are recommended)?
- Is the treated eye the WORSE seeing eye?
- Does the patient agree that they DO NOT receive continuing benefits from treatment?

Permanent discontinuation of anti-VEGF treatment recommended if:
- Visual acuity < 15 letters (absolute) on 2 consecutive visits despite optimum treatment AND
- Attributable to wet AMD in the absence of other pathology

Cataracts
- If a patient is scheduled for a cataract operation within the next 3 months and if it is anticipated that vision will improve due to the procedure, the above discontinuation criteria may no longer apply, and patient may continue treatment and be reassessed following their cataract operation.
- A decision support tool for wet AMD has been developed to support shared decision-making discussions with patients and is available here: https://www.england.nhs.uk/publication/decision-support-tool-making-a-decision-about-wet-age-related-macular-degeneration/

Appendix 3. Drug information and dosing details based on SPC

Figure 1. Indicative combined costs (drug and activity) based on the average number of doses from NHSE modelling and real-world NHS data at the time of writing

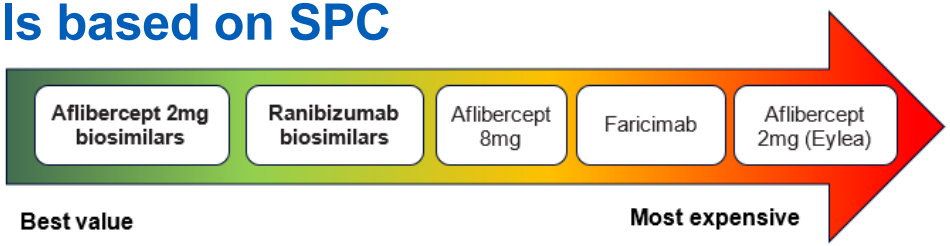


Table adapted from NHSE

Drug	Mechanism of action – receptor(s) inhibited	NICE TA for other ophthalmology indications	Posology post-loading		Treat and extend dose increment intervals	Maximum dosing intervals	Minimum dosing intervals
			No disease activity	Disease activity			
First choice options							
Ranibizumab biosimilar	VEGF-A	DMO (TA274) mCNV (TA298) BRVO/CRVO (TA283)	Treat and extend	Continue monthly	2 weeks	12 weeks	4 weeks
Aflibercept 2mg originator **Aflibercept 2mg biosimilar when available**	VEGF-A VEGF-B PLGF	*Biosimilar not available at time of TA publication* BRVO (TA409), CRVO (TA305) DMO (TA346), mCNV (TA486)	Treat and extend	Continue 2-monthly	2 – 4 weeks	16 weeks	4 weeks
Second choice options							
Aflibercept 8mg	VEGF-A VEGF-B PLGF	No published TA for any ophthalmology indication	Treat and extend	Clinical decision	Not specified	16 weeks, can be further extended to 20 weeks	8 weeks (max once monthly for 3 consecutive doses used in studies)
Faricimab	VEGF-A Ang-2	BRVO/CRVO (TA1004) DMO (TA799)	Treat and extend	Continue 8-weekly	4 weeks	16 weeks	4 weeks (3 weekly interval is off-label)
Third choice options							
Bevacizumab gamma	VEGF-A	Nil other published TA	Treat and extend	Continue monthly	Not specified	12 weeks	4 weeks
Brolucizumab	VEGF-A	DMO (TA820)	Every 3 months	Every 2 months	Not specified	12 weeks	8 weeks

Abbreviations:
DMO – diabetic macular oedema, BRVO – branch retinal vein occlusion, CRVO – central retinal vein occlusion, mCNV – choroidal neovascularisation secondary to pathologic myopia

Appendix 4. Injection frequency comparison across treatments

The table below from NHSE shows the injection frequency based on a combination of clinical trial and real-world data, supplemented by assumptions based on clinical consensus from the expert working group. Notably, there is no significant difference between treatments, except for 4-weekly ranibizumab.

Number of injections								
First choice drug	**Ranibizumab**	**Aflibercept 2mg**	**Faricimab**	**Aflibercept 8mg**	**Ranibizumab**	**Aflibercept 2mg**	**Faricimab**	**Aflibercept 8mg**
Response during maintenance phase	**Stable disease** *Regular dosing required to maintain disease activity*				**Inactive disease** *Dose intervals can be extended without affecting disease activity*			
Average treatment intervals post-loading	4 weeks	8 weeks	8 weeks	8 weeks	Treat and extend			
Year 1	13	8	7	8	7	6	6	6
Year 2	13	6	7	6	4	3	3	2
Year 3	13	7	6	7	5	3	3	3