Adult (age≥18 years) treatment pathway with anti–vascular endothelial growth factor therapy for wet age-related macular degeneration based on NICE TAs 155, 294, 672, 800 & 1022 NHSE guidance[1] and local agreements

Does the patient have **Wet age-related macular degeneration (w-AMD)?**

Does the patient meet NICE initiation criteria for of Anti–vascular endothelial growth factor (anti-VEGF) therapy?
Do all 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 (VA) changes

no

NICE criteria do not apply – Pathway not applicable

Consider SWITCH (note 5) or STOP (note 9)

yes

First choice**: Aflibercept 2mg (switch to biosimilar when available) [TA294], ranibizumab biosimilar [TA155]**
Second choice**: Aflibercept 8mg** (preferred), faricimab [TA800]
Third choice: Bevacizumab gamma [TA1022], brolucizumab [TA672])

Assess response post-loading (monthly injections) **before 4th injection** (see Table 2)
Check injections were administered as per schedule

Optimal response
- BCVA: improvement or stabilisation AND
- OCT: no disease activity

CONTINUE and **EXTEND** intervals (see Table 2)

Suboptimal response
Improvement in disease activity on OCT but with signs of active disease. E.g.
- OCT: anatomical features of active disease (e.g. fluid in retina, new haemorrhage or SRHM)

CONTINUE with **REGULAR** intervals (see Table 2)
SWITCH if active disease 4-8 weeks after last injection

Poor response
- BCVA: < 25 letters (absolute) attributable to wet AMD on 2 consecutive visits

STOP treatment. **SWITCH** if clinically indicated (see Note 9)

MAINTENANCE PHASE

Subsequent injections with visual acuity and OCT assessments
(minimum visual acuity and OCT checks per visit)

CONTINUE scheduled prescribing and MONITOR

Treatment burden (e.g. unable to safely extend treatment intervals > 7 weeks)

Drug related adverse reaction

Consistent responses after 2 to 3 monitoring visits (see Note 6)
Check injections were administered as per schedule and responses not attributable to other causes

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 reactivation or disease activity

EXTEND intervals (normally extend by 2-4 weeks, maximum up to 3-5 months) if extension not recently attempted based on disease activity (refer to Table 2 for individual drug posology)

Consider **PAUSE** in inactive disease after maximum extension or in stable disease (see Notes 7 and 8)

MAINTAIN current interval if disease is known not to improve with shorter intervals and worsens with longer intervals. If the patient failed at least **TWO** extended interval attempts and there is no clinical benefit, **SWITCH BACK** to previous anti-VEGF if it is more cost-effective and clinically appropriate (see Note 5)

Suboptimal response or unstable disease
No improvement in BCVA OR improvement in anatomical features but signs of persistent activity. E.g.
- BCVA worsens/ no improvement (≤5-letter improvement) OR
- OCT: anatomical features of persistent active disease (e.g. non resolving fluid in retina, new haemorrhage or SRHM)

REDUCE intervals (see Table 2)

SWITCH after 3 consecutive monthly injections (see Note 5)

At any point of treatment, consider STOP (see Note 9) if:
Reduction of BCVA to < 25 letters (absolute) attributable to wet AMD on 2 consecutive visits

Is response at 12 months since start of treatment with each line of treatment (see Note 10) adequate?
Check whether ongoing treatment is still clinically appropriate, based on OCT results, visual function tests and perceived patient benefit (see Notes 5 and 6). Changes In OCT precedes visual function tests. Indicators of inadequate response include:
- BCVA < 25 letters on 2 consecutive visits attributable to wet AMD in the absence of other pathology
- Persistent disease activity despite optimal treatment

YES

NO

STOP or **SWITCH** treatment (see Note 9).
Recommend a **maximum of THREE lines of therapy** to be commissioned per eye, with the expectation that the **first anti-VEGF used should normally be first choice options**

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Approved by Herts and West Essex Area Prescribing Committee July 2025

Adult (age≥18 years) treatment pathway with anti–vascular endothelial growth factor therapy for wet age-related macular degeneration based on NICE TAs 155, 294, 672, 800 & 1022 NHSE guidance[1] and local agreements

Pathway adapted from NHS England (2025). Commissioning Guidance: Medical Retinal Treatment Pathway in Wet Age-Related Macular Degeneration (v1.1). Available at: https://future.nhs.uk/connect.ti/nhsbiosimilarhub/ login required

Table 2. Drug dosing details according to SPC recommendations

Drug	Cost tier	Posology post-loading		Treat-and-extend dose increment intervals	Maximum treatment intervals	Minimum dose intervals
		No disease activity	Disease activity			
First choice						
Ranibizumab biosimilar	£	Treat-and-extend	Continue monthly	2 weeks	12 weeks	4 weeks
Aflibercept 2mg Biosimilar once available	£££ £		Continue 2-monthly	2-4 weeks	16 weeks	4 weeks
Second choice						
Aflibercept 8mg	££	Treat-and-extend	Clinical decision	Not specified	16 weeks, can be further extended to 20 weeks	8 weeks (max once weekly for 3 consecutive doses in used studies)
Faricimab	£££		Continue 8-12 weekly	4 weeks	16 weeks	21 days
Third choice						
Bevacizumab	£££	Treat-and-extend	Continue monthly	Not specified	12 weeks	4 weeks
Brolucizumab	NE	Every 3 months	Every 2 months	Not specified	12 weeks	8 weeks

Cost tier per annum (drug and activity) based on average number of doses- **£** (cheapest), **£££** (most expensive) from NHSE modelling and real-world NHS data at the time of writing.

NE: Not evaluated

Notes and recommendations for best practice to be read in conjunction with pathway

Note 1: Treatment goals

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

However, it is recognised that not all patients can achieve complete disease remission despite frequent and timely dosing due to the progressive nature of the disease.

Recommendations for best practice:

At the beginning of the treatment, communicate with patients at treatment initiation of all treatment possibilities at the outset. This would include:

- *Expected treatment outcomes and treatment burden with patients. Use real-world data to support communication, especially those with "poor" vision.*
- *Potential treatment changes throughout their journey, including the use of best value medicines when available.*
- *Potential for stopping treatment if there is no further clinical benefit with continued treatment.*

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/

Note 2: Service delivery by other healthcare professionals

Some SPCs (e.g. Ongavia®) mandate administration by "a qualified ophthalmologist experienced in intravitreal injections". However, in practice this may be administered by a suitably trained healthcare professional (HCP). RCOphth 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*.'

In such circumstances, intravitreal injections performed by the HCP will be 'off-label'. Local governance processes should be in place to manage any ophthalmological or medical complications.

Note 3: Use of anti-vascular endothelial growth factor (VEGF) outside the NICE visual acuity criteria – This criteria has not been agreed within HWE ICS therefore not applicable to this pathway.

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Note 4: Choice of therapy

If more than one treatment option is suitable and service capacity allows for timely treatment, choose the least expensive (taking into account administration costs, frequency and commercial arrangements).

Clinicians are advised to consider the patient's medical history, existing treatment in the other eye (if receiving treatment) and patient factors.

Medicines and Healthcare Regulatory Agency (MHRA) recommends brand name prescribing. If more than one biosimilar brand is available, choose best value brand available locally.

Recommendations for best practice:

Where clinically appropriate, use aflibercept 2mg (switch to biosimilar once available) and ranibizumab biosimilar as first choice options.

Examples of specific clinical considerations where aflibercept or ranibizumab may not be appropriate:

- Non-responder to ranibizumab/ aflibercept in fellow eye previously
- Ranibizumab-specific contraindications: subretinal bleed >50% of lesion, idiopathic polypoidal choroidal vasculopathy [PCV]

Use aflibercept 8mg and faricimab as second choice options. This is usually when high injection frequency is not acceptable with first choice options

The following patient groups may be better managed with the least number of injections which will outweigh the cost:

- learning difficulties
- dementia
- hospital transport
- requiring treatment in the operating theatre under sedation/deep sedation/general anaesthesia
- frequent inpatient hospital admissions or other regular attendance (e.g. chemotherapy)

Clinical factors where aflibercept 8mg or faricimab might be first choices

- Non-responder to first-line choices in fellow eye previously
- Treatment harmonisation (see recommendation below)

Use brolucizumab and bevacizumab gamma (licensed) as third choice options.

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).

Note 5: Consider treatment switch if:

- 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

Recommendations for best practice:

If the patient failed at least TWO extended interval attempts and there is no clinical benefit, switch back to 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.

When switching to a different anti-VEGF, it would be a clinical decision to determine whether reloading is required. RCOphth guidance recommends the following:

Loading with new agent recommended (within product license):

- those in whom the treatment interval cannot be extended beyond 7 weeks with the current agent.

Loading with new agent may not be required (off label use):

- those managed on longer intervals (8 or more weeks) to reduce treatment burden. These patients may be switched to new agent on a matched treatment interval followed by a treat-and-extend interval post-initial dose

This approach may be easier for patients, but it is not known whether loading these patients may increase the chances of further extension so reload may also be considered.

It is recommended that a maximum of THREE lines of therapy should be commissioned per eye, with the expectation that the first anti-VEGF used should normally be first choice options [i.e. aflibercept 2mg (biosimilar when available) or ranibizumab biosimilar].

Subsequent lines of therapy can be second or third choice options depending on individual circumstances.

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
- Switch if ranibizumab biosimilar used first line to aflibercept 2mg biosimilar [locally agreed]

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Note 6: Confounding factors in response assessments

Be aware that 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 (see also Note 11)

Note 7: Disease activity in the long term

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)

Note 8: Treatment pause

Clinicians may consider temporarily withholding treatment if:

- no disease activity [i.e. disease has become inactive on maximum extension (usually 3 to 5 months intervals depending on the drug- see Table 2 for details) after 2-3 doses]

RCOphth guidance (section 10.4) recommends monitoring with visual acuity and OCT for disease reactivation. Although there is no data on length of monitoring period required, there is consensus that patients should be monitored for at least 2 years after disease stability is achieved. If there is recurrence of disease activity, treatment is reinstated until disease stabilisation is achieved, as indicated by best corrected visual acuity and/or lesion morphology.

Note 9: Stopping treatment (e.g. permanent discontinuation)

Recommendations for best practice:

REVIEW with consideration to stop treatment if:

- visual acuity < 25 letters (absolute) on 2 consecutive visits despite optimum treatment (see also Note 6 and 11) 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.

Questions to be considered when deciding whether further treatment is beneficial (discontinue treatment 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?

Treatment STOP recommended if:

- *visual acuity < 15 letters (absolute) on 2 consecutive visits despite optimum treatment (see also Note 6 and 11) AND*
- *attributable to wet AMD in the absence of other pathology*

Where a decision is made to discontinue treatment permanently where risks of giving injections outweigh its potential benefits, no further monitoring is required for that eye. These patients may be discharged from the hospital eye service (refer to RCOphth guidance section 10.5 for further information).

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-wetage-related-macular-degeneration/

Note 10: Initial 12-month and annual response assessments

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)

Changes in OCT precedes visual function tests

Recommendations for best practice:

Consider treatment switch (see Note 5) or permanent discontinuation (see Note 9) if:

- *BCVA < 25 letters on 2 consecutive visits attributable to wet AMD in the absence of other pathology (see also Note 6 and 11) OR*
- *Persistent disease activity despite optimal treatment*

Note 11: Cataracts

Recommendations for best practice:

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, discontinuation criteria may no longer apply, and patient may continue treatment.

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Note 12: Anti VEGF adverse events (from HWE ICS APC December 2022 wet AMD pathway)

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. *See individual SPC's for other adverse events and further prescribing information.*

Brolucizumab may cause intra-ocular inflammation[1]. Due to this, it is not suitable for remote clinics, initial bilateral administration, patients with a previous history of uveitis, vision in only eye or history or vein occlusion. Patients must receive information and be counselled on the adverse effects of brolucizumab (to be documented in the patient notes). Clinical staff must exclude history of prior intra-ocular inflammation and should use a red flag questionnaire after each injection to identify signs and symptoms of intra-ocular inflammation. Patients with positive symptomatology would then be further screened with slit-lamp examination supported with widefield retinal imaging if deemed appropriate. Further brolucizumab treatment should be withheld in cases with retinal vasculitis/vascular occlusion.

Abbreviations & Explanations

AMD	Age-related Macular Degeneration
BCVA	Best Corrected Visual Acuity
OCT	Optical Coherence Tomography
RCOphth	The Royal College of Ophthalmologists
SPC	Summary of Product Characteristics
VA	Visual Acuity
VEGF	Vascular Endothelial Growth Factor
wAMD	Wet Age-related Macular Degeneration

Definitions

Term	Explanation
Fellow eye	The eye opposite the one being treated
Line of therapy	The order in which different therapies are given to people as their disease progresses. 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 switchback 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.
Recommendations for best practice	Recommendations made by the expert working group following review of real-world evidence or based on consensus from expert working group. These are subject to local commissioning agreements.
Stopping treatment/ permanent discontinuation	A point in the patient's treatment journey where clinicians decide to stop treatment permanently. This is usually when further treatment is unlikely to benefit the patient.
Treatment harmonisation	The act of using only one drug for both eyes. Usually occurs when one eye is already on treatment, but the other eye qualifies for another treatment.
Treat and extend protocol	A standard treatment regimen for treating wAMD, where the interval for the next anti-VEGF injection is extended by 2 to 4 weeks up to a maximum of 20 weeks depending on the anti-VEGF used.
Treatment pause	A point in the patient's treatment journey where clinicians decide to temporarily withhold treatment. This is usually when the disease has become inactive whilst the patient is on a drug with maximum dose extension intervals.
Worse-seeing eye	Also known as the weaker eye. This occurs when one eye sees significantly better than the other eye.

References:

1. www.medicines.org.uk Beovu 120mg/ml solution for injection https://www.medicines.org.uk/emc/product/11145/smpc

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