CONSULTATION DRAFT

Enclosure No:	x/XXXXX/0726
Agenda item No:	xx – All Wales wet (neovascular) age-related macular degeneration prescribing guidelines
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1.0 Action for consultees

Consultees are asked to consider and comment on the *All Wales wet (neovascular) age-related macular degeneration prescribing guidelines*. Consultees are also asked to consider the accompanying equality and health impact assessment (EqHIA) form.

2.0 Purpose

During the 2025–2026 financial year, NHS Wales spent over £28m on anti-VEGF treatment for retinal conditions, with approximately 77,000 injections administered. The expected increase in incidence and prevalence of wet age-related macular degeneration over the next 10 years will require ophthalmology services to continue to innovate and provide cost-effective, streamlined services to maximise capacity and meet demand.

The purpose of this pathway is to help NHS Wales to realise the benefits of biosimilar anti-VEGFs for people with wAMD and services by promoting treatment consistency across health boards and facilitating the planning of medicines procurement.

The resources are pertinent to the following AWMSG ambitions, set out in the AWMSG Strategy for Wales: 2024–2029:

- Help people in Wales get the best outcomes from medicines
- Optimise the value that NHS Wales achieves from its investments in medicines

2.1 Process

- June 2026: Draft document considered by AWPAG
- July–August 2026: Draft document out for consultation
- *September 2026: Consultation comments and responses considered by AWPAG for sign-off*
- *November 2026: Document presented to AWMSG for endorsement*

2.2 Consultees

Consultees include, but are not limited to:

- Directors of Pharmacy
- Medical Directors
- Assistant Medical Directors
- Health Board Chief Executives
- Directors of Nursing
- Local Medical Committees
- Directors of Public Health
- General Practitioners Committee (GPC) Wales
- Royal College of General Practitioners (RCGP)
- British Medical Association (BMA) Cymru
- Llais Cymru
- Community Pharmacy Wales (CPW)
- Public Health Wales (PHW)
- Welsh Government
- NHS Wales Joint Commissioning Committee (JCC)
- National Institute for Health and Care Excellence (NICE)
- AWMSG members and deputies
- AWPAG members and deputies

1.0 Introduction

1.1 Background

Degeneration of the macular and posterior pole was the cause of around 3% of certifications for visual impairment or blindness in the UK in 2009–2010.[1] In a 2012 study, wet age-related macular degeneration (wAMD; also known as neovascular AMD) was estimated to affect 263,000 people in the UK,[2] with the prevalence predicted to rise to 339,000 by 2020.[2] Further projections suggest prevalence could increase to 683,000 by 2050.[3]

A significant reduction in blindness registrations due to wAMD was noted following the 2007 introduction of intravitreal anti-vascular endothelial growth factor (VEGF) therapies in the UK and Europe. Data from Denmark found that incidence of legal blindness from AMD in people over 50 years decreased by 50% between 2000 and 2010, with the majority of the reduction coinciding with the introduction of anti-VEGF treatments.[4]

During the 2025–2026 financial year, NHS Wales spent over £28m on anti-VEGF treatment for retinal conditions, with approximately 77,000 injections administered. However, the expected increase in incidence and prevalence of wAMD over the next 10 years will require ophthalmology services to continue to innovate and provide cost-effective, streamlined services to maximise capacity and meet demand.

1.2 Development of the guidelines

The impetus for the development of these guidelines comes from the National Clinical Strategy for Ophthalmology: Delivering the future of ophthalmology in Wales. This strategy tasked the Medical Retina and Uveitis Clinical Reference Group with implementing nationally agreed clinical pathways across all health boards and has coincided with the availability of biosimilars for ranibizumab and aflibercept following the loss of patent exclusivity. No more anti-VEGF patent expiries are expected until 2034 at the earliest. Therefore, the Medical Retina and Uveitis Clinical Reference Group are taking the opportunity to rationalise the use of anti-VEGFs in the treatment of eye disorders to maximise the benefits in an equitable manner across NHS Wales.

1.3 Purpose

The purpose of these guidelines is to help NHS Wales to realise the benefits of biosimilar anti-VEGFs for patients and services by promoting treatment consistency across health boards and facilitating the planning of medicines procurement.

The aim is to agree general principles for starting, pausing and stopping treatment, the choice of treatment, and treat-and-extend (TREX) rules that can be applied for any medicine used in the different clinic setups in different units across NHS Wales.

The guidelines are for the use of medical and clinical staff and provide information for NHS commissioners and governance.

2.0 Treatment criteria

2.1 Inclusion criteria for initial treatment

To be eligible for treatment, patients should fulfil the following criteria (National Institute for Health and Care Excellence [NICE] technology assessments [TAs] TA294, TA155, TA800, TA1022, TA672):

- Best corrected visual acuity (BCVA) of between 6/12 and 6/96*
- No permanent structural damage to the central fovea
- Lesion size of less than or equal to 12-disc areas in greatest linear dimension
- Active disease with evidence of recent presumed disease progression

NICE guideline (NG) 82 (not mandatory) recognises the use of anti-VEGFs outside of the criteria set out in NICE TAs:

- In eyes with visual acuity (VA) of 6/96 or worse, consider treatment if evidence of VA better than 6/96 in preceding six weeks, especially when better seeing eye is affected.
- Be aware that treatment for eyes with evidence of active wAMD and VA better than 6/12 is clinically effective and may be cost effective depending on the regimen used.

3.0 Treatment options

3.1 First line

First-line options are aflibercept 2 mg biosimilar and ranibizumab 0.5 mg biosimilar, where clinically appropriate.

3.2 Second line

Aflibercept 8 mg and faricimab 6 mg are second-line options. These may also be appropriate first-line options in situations where:

- there are contra-indications, or the other eye has had a poor previous response, to aflibercept 2 mg and ranibizumab,
- treatment harmonisation is required and the other eye is being treated with aflibercept 8 mg or faricimab,
- the person is unable to tolerate frequent injections (e.g. due to learning difficulties, dementia, hospital transport requirements, operating theatre administration under sedation, deep sedation or general anaesthesia required, or co-morbidities requiring frequent hospital admissions or appointments),
- there are atypical lesions (e.g. polypoidal choroidal vasculopathy, retinal angiomatous proliferation),
- there are service capacity constraints.

Where either medicine would meet the patient's needs, the treatment choice should be based on the medicine with the lowest acquisition cost.

3.3 Third line

Bevacizumab gamma and brolucizumab are third-line treatment options when first- and second-line options fail or are contraindicated. Use is limited due to the safety profile (brolucizumab inflammation risk) or higher cost (bevacizumab gamma).

* See Appendix 1 for conversion to early treatment diabetic retinopathy study (ETDRS) letters score and LogMAR value.

Guidance from the Royal College of Ophthalmologists (RCOphth) notes that “very few patients with active wet AMD do not respond to anti-VEGF therapy.” Therefore, in cases of non-response, diagnosis should be confirmed using appropriate imaging where necessary.[3]

4.0 Treatment regimen

Following assessment of initial response, the TREX approach is preferred for most patients. The general principle with a TREX protocol is to achieve the best visual and anatomical improvement possible and to maintain those gains with as few injections as possible (i.e. the longest possible interval between injections that maintains those gains). Figure 1 provides an overview of the treatment pathway.

4.1 Loading phase

Patients are treated initially with monthly injections (loading doses) based on criteria in the medicine’s Summary of Product Characteristics (SmPC). After monthly loading doses, assess response (see 4.1.1) and adjust interval accordingly (see 4.2.1).

4.1.1 Assessing response

Following completion of the loading phase, NHS England advice[5] recommends assessing response and managing ongoing treatment as follows:

- Optimal response (BCVA improvement or stabilisation; optical coherence tomography (OCT) shows no disease activity) – continue treatment and extend intervals.
- Suboptimal response (BCVA improvement or stabilisation; improvement in disease activity on OCT but with signs of active disease) – continue with regular intervals; switch if active disease 4–8 weeks after last injection.
- Poor response (BCVA < 25 letters [absolute] attributable to wAMD on two consecutive visits) – stop treatment. Switch if clinically indicated.

4.2 Maintenance phase

During the maintenance phase, VA and OCT assessments should be completed at each injection visit.

The follow-up interval should be extended to find the maximum interval between injections that maintains the visual and anatomical gains. The interval is extended by 2 to 4 weeks at the clinician’s discretion, up to a maximum of 12 to 20 weeks based on disease activity and the medicine’s licensed dosing intervals.

The maximum response is achieved either if there is no fluid on OCT scanning, and no other signs of activity (e.g. haemorrhage). In some cases, sub-retinal fluid (SRF) or intra-retinal fluid (IRF) may persist despite monthly injections. If fluid persists, the maximum response is considered to be when there is no further anatomical improvement after two consecutive treatments at 4-week intervals.

4.2.1 Interval criteria

Extend the interval if:

- Stable or better vision or VA loss not due to disease activity AND
- OCT scan shows no sign of fluid, or stable fluid that does not decrease at shorter treatment intervals OR
- No disease reactivation or disease activity AND
- Extension not previously, or not recently, attempted

For aflibercept 8 mg or faricimab consider 4-week extension intervals in the first instance. For aflibercept 8 mg, interval extensions of more than 4 weeks may be considered at the discretion of the reviewing clinician, in consultation with the person.[6]

If a recent extension failed, consider maintaining at shorter interval before attempting extension again.

Maintain the interval if:

- Stable or better vision or VA loss not due to disease activity AND
- OCT scan shows no sign of fluid, or stable fluid that does not decrease at shorter treatment intervals but does increase with longer intervals.

If a recent extension resulted in disease reactivation, then return to the last known interval that offered disease stability. Consider fixing the interval for three further doses before any subsequent attempt to extend (e.g. if recent reactivation at 12-week interval, maintain at 10-week interval for ~3 visits before attempting extension again).

Reduce the interval if:

- VA reduced by 5 or more letters due to disease activity AND/OR
- OCT or examination shows signs of increased disease activity: new/worsening fluid (SRF/IRF/sub-retinal pigment epithelium) OR subretinal hyperreflective material OR new macular haemorrhage

If the patient is being treated with aflibercept 8 mg or faricimab but there is no clinical improvement, or if extension of the treatment interval cannot be achieved, consider switching the person back to their original preparation (aflibercept or ranibizumab biosimilar).

Review/assess patients after 12 months of injections and at least annually thereafter.

4.2.2 Cataracts

If the person has poor fundus view and is listed for cataract surgery, continue treatment at every visit until after surgery and, if possible, expedite surgery.

4.3 Switching and stopping treatment to reduce treatment burden

4.3.1 Switching treatment

When switching to a different anti-VEGF, it would be a clinical decision to determine whether reloading is required. RCOphth guidance[7] recommends the following:

- Loading with new agent **may** be required (within product licence) for 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 depending on medicine) for those managed on longer intervals (8 or more weeks) where switching aims to reduce treatment burden. These people may be switched to new agent on a matched treatment interval followed by a TREX 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.

4.3.2 Pausing treatment

With TREX, the maximum interval between injections is generally 16 weeks. With some newer agents, interval extension may be up to 24 weeks. If disease remains inactive at a ≥ 16-week interval, patients should be maintained at that interval for 2–3 further injections. If the wAMD remains inactive after a third interval of ≥ 16 weeks, consider pausing treatment to evaluate ongoing disease activity.

Once treatment has been paused, it is prudent to monitor at shorter intervals initially (6–8 weeks), extending the monitoring interval up to 16 weeks if the disease remains inactive.[8]

Once no longer receiving injections and stable for approximately 3 months, further monitoring in the hospital outpatient clinic or virtual clinic should be considered.

Once stable off treatment for 12 months, the patient can be discharged from the hospital eye service. Further community follow-up may be with their local optometrist or a Welsh General Ophthalmic Services 4 (WGOS4) optometrist for monitoring with advice on self-monitoring.

RCOphth guidance (section 11.3) states that 'Although there is no data on length of monitoring period required, there is consensus that patients should be monitored for at least two years after disease stability is achieved'.[7]

4.3.3 Restarting treatment

If treatment was stopped less than 9 months ago, patients can go straight into a TREX regimen starting at 6-week intervals. Reloading is recommended if restarting more than 9 months after last injection.

However, the decision to reload or not should be based on clinical assessment and the clinician's decision should prevail.

4.3.4 Stopping/discontinuing treatment

Stopping treatment should be considered if a person develops central retinal atrophy or scarring, such that there is no prospect of functional improvement, or if they develop hypersensitivity to anti-VEGF agents.

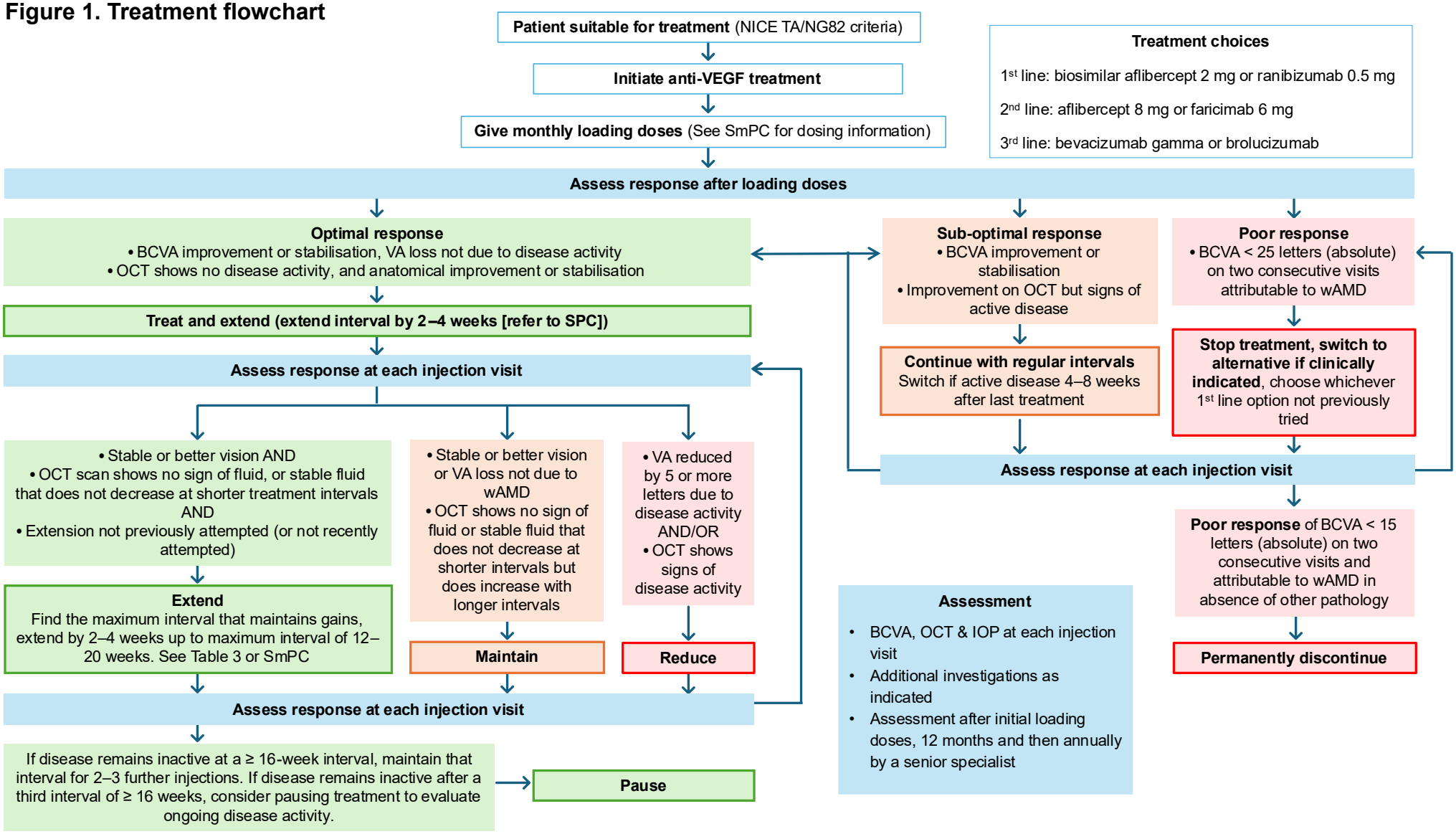
In general, with VA < 30 early treatment diabetic retinopathy study (ETDRS) letters, discontinuing treatment should be considered.

In patients with a VA < 15 ETDRS letters (attributable to macular pathology), treatment should be discontinued.

In patients with inactive/scarring, consider discharge to patient-initiated follow-up with annual optometry monitoring.

If an adverse drug reaction occurs – report it to the Medicines and Healthcare products Regulatory Agency (MHRA) Yellow Card Reporting Scheme (https://yellowcard.mhra.gov.uk/).

207 **Figure 1. Treatment flowchart**



5.0 Harmonisation of treatment

Where wAMD is present in only one eye, OCT monitoring should be carried out in both eyes at every visit, where capacity allows. This will facilitate early identification and treatment in the other eye, which is associated with better outcomes. OCT monitoring will not be required in an eye with end stage disease that will therefore not benefit from treatment.

6.0 Intravitreal administration by other healthcare professionals

Some SmPCs direct administration by a qualified ophthalmologist experienced in intravitreal injection, and while RCOphth guidance acknowledges this, it also supports administration by a suitably trained healthcare professional (HCP). In addition, the RCOphth 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.'[9]

In such circumstances, intravitreal injections performed by the HCP will be unlicensed and local governance processes should be in place to manage this.

7.0 Licensed dose and interval recommendations[5]

Table 3. SmPC dose and interval recommendations[10,11]

Medicine	Posology post-loading		TREX dose increment intervals	Maximum treatment intervals	Minimum dose intervals
	No disease activity	Disease activity			
First line					
Aflibercept 2 mg biosimilar	TREX	Continue 2-monthly	2–4 weeks	16 weeks	4 weeks
Ranibizumab biosimilar		Continue monthly	2 weeks	12 weeks	4 weeks
Second line					
Aflibercept 8 mg	TREX	Clinical decision	Not specified	4 months, can be further extended to 6 months	4 weeks
Faricimab		Clinical decision	Up to 4 weeks	16 weeks	4 weeks*
Third line					
Bevacizumab gamma	TREX	Continue monthly	Not specified	12 weeks	4 weeks
Brolucizumab	TREX or treatment every 3 months	Every 2 months	Up to 4 weeks	12 weeks	8 weeks

Unlicensed dosing details

*Faricimab unlicensed dosing: 3-weekly dosing was used in studies to allow flexibility of dose scheduling.[12]

The safety and efficacy of unlicensed dosing has not been evaluated.

8.0 Abbreviations

AMD	Age-related macular degeneration
BCVA	Best corrected visual acuity
ETDRS	Early treatment diabetic retinopathy study
HCP	Healthcare professional
IRF	Intra-retinal fluid
MHRA	Medicines and Healthcare products Regulatory Agency
NG	NICE guideline
NICE	National Institute for Health and Care Excellence
OCT	Optical coherence tomography
RCOphth	Royal College of Ophthalmologists
SmPC	Summary of Product Characteristics
SRF	Sub-retinal fluid
TA	Technology assessment
TREX	Treat-and-extend
VA	Visual acuity
VEGF	Vascular endothelial growth factor
wAMD	Wet age-related macular degeneration (also known as neovascular age-related macular degeneration)
WGOS4	Welsh General Ophthalmic Services 4

9.0 References

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Appendix 1: Conversions between letter, LogMAR and Snellen VA scores[13]

ETDRS letters	LogMAR value	Snellen equivalent (feet)	Snellen equivalent (metres)
5	1.6	20/800	6/240
10	1.5	20/640	6/190
15	1.4	20/500	6/150
20	1.3	20/400	6/120
25	1.2	20/320	6/96
30	1.1	20/250	6/75
35	1	20/200	6/60
40	0.9	20/160	6/48
45	0.8	20/125	6/38
50	0.7	20/100	6/30
55	0.6	20/80	6/24
60	0.5	20/63	6/19
65	0.4	20/50	6/15
70	0.3	20/40	6/12
75	0.2	20/32	6/9
80	0.1	20/25	6/7.5
85	0	20/20	6/6
90	-0.1	20/15	6/5
95	-0.2	20/12	6/4

Adapted from Beck et al. (2003).[13]