
Guidelines for the treatment of wet AMD with anti-VEGF agents

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Document history

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Abbreviations

AMD	Age-related macular degeneration
Anti-VEGF	Anti-vascular endothelial growth factor
BCVA	Best corrected visual acuity
ETDRS	Early Treatment Diabetic Retinopathy Study
FFA	Fundus fluorescein angiography
ICG	Indocyanine green angiography
IOI	Idiopathic orbital inflammation
IRF	Intraretinal fluid
OCT	Optical coherence tomography
OCTa	Optical coherence tomography angiography
PCV	Polypoidal choroidal vasculopathy
PED	Pigment epithelial detachment
RPE	Retinal pigment epithelium
SRF	Subretinal fluid
TA	Technology appraisal
VA	Visual acuity
VEGF	Vascular Endothelial Growth Factor

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1 Background and scope

1.1 Background

Age-related macular degeneration (AMD) is the term given to ageing changes without any other obvious cause that occurs in the central area of the retina (macula), sometimes with new blood vessel formation (wet AMD). The consequences of this condition for vision can be severe. AMD is the most common cause of visual impairment in the developed world, and the Royal National Institute of Blind People (RNIB) reports that AMD is the most common cause of certification for vision impairment.

Anti-vascular endothelial growth factor (VEGF) medications – developed following recognition of the key role that VEGF plays in wet AMD pathogenesis – are highly effective, and the established treatments of choice for wet AMD. Anti-VEGF medications for wet AMD are given as an injection into the eye (intravitreal injection).

According to NHS England, eyecare is the highest volume outpatient specialty within the NHS and the medicines used for medical retinal vascular conditions account for some of the highest cost and volume treatments used within secondary care.

Due to increasing life expectancy and an ageing population, the NHS expects that demand for medical retinal vascular treatments will continue to increase as more patients with eye disease are diagnosed and treated. Continually rising demand has also impacted ophthalmology outpatient services, worsened by the coronavirus (COVID-19) pandemic.

There are currently four licensed intravitreal anti-VEGF drugs recommended by NICE technology appraisal guidance as options for the treatment of wet AMD¹:

- Ranibizumab ([TA155](#); 2008)²
- Aflibercept ([TA294](#); 2013)³

¹ A sixth anti-VEGF agent known as pegaptanib is not recommended by NICE for the treatment of wet AMD (TA155; 2008).

² In 2022 and 2023, 3 ranibizumab biosimilars were licensed, (Ongavia, Byooviz and Ximluci). Equivalent safety and efficacy to the reference product ranibizumab (Lucentis) has been confirmed in phase III clinical trials in eyes with treatment naïve neovascular AMD.

³ In 2013, NICE TA294 evaluated aflibercept 2mg for wet AMD. In 2024, a high-dose formulation of aflibercept (i.e., 8mg) for wet AMD was granted marketing authorisation. [NICE](#) concluded that aflibercept 8mg was not eligible for TA guidance and should be considered for routine commissioning because it is clinically equivalent and of at least equal cost-effectiveness to the aflibercept 2mg formulation. In 2025, 2 aflibercept 2mg biosimilars were licensed, (Eydenzelt and Mynzepli). Equivalent safety and efficacy to the reference product aflibercept (Eylea) has been confirmed in phase III clinical trials in eyes with treatment naïve neovascular AMD.

- Brolucizumab ([TA672](#); 2021)
- Faricimab ([TA800](#); 2022).

Eligibility criteria for treatment with these agents are detailed in Box 1.

NHS England have also developed [commissioning recommendations](#) for intravitreal anti-VEGF treatments in England for medical retinal conditions (2023). In addition, NHS England have published [NHS England » Commissioning framework for best value biological medicines](#) which supports the use of biosimilars and SERMOG Recommendations for [biosimilars](#) are also available.

Box 1 – Eligibility criteria for treatment with anti-VEGF agents

According to NICE TA guidance, ranibizumab, aflibercept, brolucizumab and faricimab are recommended as options for treating wet AMD in adults if:

- Best-corrected visual acuity is between 6/12 and 6/96, and
- No permanent structural damage to the central fovea, and
- Lesion size is less than or equal to 12-disc areas in greatest linear dimension, and
- Evidence of recent presumed disease progression (blood vessel growth, as indicated by fluorescein angiography, or recent visual acuity changes)
- They are provided by the manufacturer with the discount agreed in the patient access scheme/ commercial arrangement.

If the patients and their clinician consider there to be more than 1 suitable treatment, the least expensive treatment should be chosen, taking into account administration costs, dosage, price per dose and commercial arrangements.

Treatment should be continued only in people who maintain adequate response to therapy.

Criteria for discontinuation should include persistent deterioration in visual acuity and identification of anatomical changes in the retina that indicate inadequate response to therapy.

1.2 Scope

- Ranibizumab, aflibercept, brolucizumab and faricimab are commissioned by NHS Kent and Medway according to NICE criteria; anti-VEGF treatment for eyes with late AMD (wet active) and visual acuity better than 6/12 is not routinely funded.
- Off-label use of licensed medicines (i.e., bevacizumab) is out of scope and not included in these guidelines.
- These guidelines will apply to all clinical staff involved with intravitreal injections of anti-VEGF agents for the treatment of wet AMD at providers commissioned by NHS Kent and Medway.
- These guidelines do not restrict a clinician’s ability to make the most appropriate decision for an individual patient through shared decision making, taking account of the patient’s needs and wishes, relevant NICE technology appraisal guidance and Kent and Medway formularies; medicines (or dosages/ dosing schedules) not included on Kent and Medway formularies (which are aligned with NICE technology appraisal guidance) need to be considered through the agreed local approval process.

1.3 Purpose

The aim of these guidelines is to improve the quality of care given to patients by:

- Setting out a consistent approach to providing anti-VEGF treatments for wet AMD across Kent and Medway to reduce variation in access to NHS services and allow fair and equitable treatment for all local patients.
- Reduce the number of patients who should be but are not currently treated or are being treated sub-optimally; and reduce the number of patients who are treated, but for whom treatment is inappropriate or ineffective.
- Make best use of NHS resources by consistently using the most clinically appropriate and cost-effective treatments and ensuring that patients receiving treatment are responding.

1.4 Review and monitoring

Monitoring of this guidance may include commissioned audits, detailed data analysis or other focussed study.

This guidance will be reviewed in response to new information that is likely to have a material effect on the current guidance, including new national guidance, research evidence or risks prompted by incident review.

2 Treatment selection

2.1 Patients commencing treatment for wet AMD

According to NICE technology appraisal (TA) guidance, ranibizumab, aflibercept, brolucizumab, and faricimab are all suitable options for the treatment of wet AMD when used in accordance with the criteria outlined in Box 1. This includes only treating patients with visual acuity between 6/12 and 6/96 and using the least expensive option if patients and their clinicians consider more than one treatment to be suitable.

In eyes with VA of 6/96 or worse, consider anti-VEGF treatment for late AMD (wet active) 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)⁴.

Anti-VEGF treatment for eyes with late AMD (wet active) and visual acuity better than 6/12 is not routinely funded.

In line with [NHS England recommendations](#) (2023):

- Subject to the criteria specified in the relevant NICE TA guidance, clinicians should consider ranibizumab biosimilar where this is clinically appropriate and there is capacity to do so.
- If ranibizumab biosimilar is contra-indicated or not clinically appropriate for the specific patient, or if there are specific clinical considerations (such as non-responder to ranibizumab in fellow eye previously, subretinal bleed >50% of lesion, idiopathic polypoidal choroidal vasculopathy [PCV]) then, subject to the criteria specified in the relevant NICE TA guidance, clinicians should consider aflibercept, brolucizumab or faricimab.

Faricimab and aflibercept preferred for:

- Eyes previously subjected to vitrectomy/ eyes requiring vitrectomy (due to their long half-life)
- Patients who would benefit the most with respect to safety from least frequent hospital appointments e.g., elderly and/ or vulnerable patients with co-morbidities affecting compliance⁵.

Ranibizumab should be considered in patients with a poor prognosis.

⁴ In patients with advanced disease, specialist assessment is required to consider the degree of structural damage and potential benefit from treatment, especially if the patient has excellent vision in the unaffected eye and is unlikely to gain functional benefit.

⁵ Systemic comorbidities in patients with AMD may present a challenge for on-going care of this long-term condition due to difficulties in accessing care and maintaining compliance. Key co-morbidities include hearing loss, poorer cognitive function, established dementia, Alzheimer's disease, depression, and anxiety related to both the diagnosis and therapy for AMD.

Aflibercept 8mg should be administered with caution in people with uncontrolled glaucoma, a significant spike in intraocular pressure (IOP) after injection and in people who have narrow angles (due to larger administration volume).

Consideration of brolocizumab as a first line treatment option should be avoided if possible. Brolocizumab has been associated with potentially serious adverse events (i.e., retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intra-ocular inflammation) that are not commonly associated with intravitreal anti-VEGF agents, and has been the subject of an [MHRA drug safety update](#).

2.2 Patients already prescribed anti-VEGF therapy for wet AMD

In line with NHS England recommendations:

- Clinicians should consider reviewing patients currently prescribed ranibizumab (Lucentis) to assess suitability to change to ranibizumab biosimilar.
- Clinicians should consider reviewing patients currently prescribed aflibercept 2mg (Eylea) to assess suitability to change to aflibercept biosimilar.

2.3 Non-responders

According to [commissioning guidance on AMD services](#) developed by the Royal College of Ophthalmologists (2024):

- The diagnosis should be re-evaluated as very few patients with active wet AMD do not respond to anti-VEGF therapy. This may require additional imaging with FFA and/or ICG angiography where applicable.
- The most likely reason for non-response is inadequate therapy due to protocol deviations. Therefore, to avoid further loss, adhere strictly to a re-loading followed by treat-and-extend protocol. Fail-safe administrative processes should be available to track patients with poor compliance due to co-morbidities.
- A switch to another anti-VEGF agent may be considered in patients with an inadequate response (see next section).

2.4 Switching criteria

- A switch to another therapy for disease control may be required for sub-optimal response after the loading phase or at any other point due to resistance to current agent (refractory cases).
- A switch to another anti-VEGF agent may be considered in cases of allergy or presumed tachyphylaxis. In a small minority, a patient may require a switch back to the previous agent or to another agent if the disease worsens after the initial switch. [NICE guideline 82](#) (2018)

recommends clinicians should consider switching anti-VEGF treatment for patients with late AMD (wet active) if there are practical reasons for doing so (e.g., if a different medicine can be given in a regimen the person prefers) but cautions that the clinical benefits [in terms of visual acuity] are likely to be limited⁶. However, some patients may potentially benefit from a treatment regimen that has fewer injections (see below).

- A switch to another agent to reduce treatment burden may be considered for individuals:
 - who respond to treatment but for whom the treatment interval cannot be extended beyond 7 weeks with the current agent. These cases may need a loading dose of the new agent before extension. Careful monitoring is required at this phase as these are difficult to treat cases.
 - managed on longer intervals (8 or more weeks) to reduce treatment burden. These cases may be switched on a matched treatment interval and then 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 offered.
- Patients (and/or their carers) should be actively involved in all decisions about the switching of treatment.
- A maximum of 2 switches are allowed. Switching between biosimilars or between a biosimilar and/the reference medicine (i.e., the originator product) will not count towards the maximum of two switches allowed. Switching between aflibercept 2mg and aflibercept 8mg (or vice versa) will also not count towards the maximum of 2 switched allowed.

Switching to a previously used anti-VEGF permitted if any of the following apply:

- As part of a switch-back strategy in year 1.
- Drug-related adverse event has occurred with current anti-VEGF e.g., endophthalmitis.
- If switching has not yielded superior outcomes in terms of vision or disease activity.
- Where an initial good response following a switch has deteriorated and the patient has become a frequent user or a sub-optimal responder.
- Where disease stability has been achieved and maintained for at least 6 months and there is a justification for switching back to a previously used anti-VEGF such as requirement for less frequent administration or low cost.

⁶ NICE guideline 82 (2018) incorporates NICE TA guidance on ranibizumab, aflibercept and pegaptanib, but not on brolucizumab or faricimab as these were published after NICE NG82 was issued.

In these cases, switching back to a previously used anti-VEGF will not count towards the maximum of two switches allowed⁷. However, repeated switches between previously used treatments should not be undertaken.

Treatment choice when switching anti-VEGF agent

If the patient and their clinician consider there to be more than 1 suitable treatment, the least expensive treatment should be chosen, taking into account administration costs, dosage/ dosing schedule, price per dose and commercial arrangements.

2.5 Discontinuation criteria

Patients (and/or their carers) should be actively involved in all decisions about the stopping of treatment.

Treatment with anti-VEGF agents should be discontinued in the following circumstances:

- In the case of stable disease. Defined here as 2–3 consecutive intervals between injections at maximal extension (i.e., 12–16 weeks)⁸ with dry retina and stable VA⁹. Treatment should be ceased and patients observed according to a ‘monitor-and-extend’ regimen. This initially involves monitoring patients with VA and OCT assessments 4 weeks after the last missed dose. If wet AMD remains inactive, the intervals between monitoring can be incrementally increased at the discretion of the treating clinician. Patients who have been monitored for 2 years without disease recurrence may be discharged with self-monitoring and annual sight tests with their local optometrist. Low-risk patients (with the exception of patients with only one treatable eye and vulnerable adults) may be considered for earlier discharge. If disease recurrence is detected, retreatment should be initiated as soon as possible. Clinicians may decide to restart the pathway or determine injection frequency based on disease severity and previous response to treatment.
- The eye develops late AMD (wet inactive)¹⁰ with no prospect of functional improvement, defined as:
 - fibrous scar, or
 - sub-foveal atrophy or fibrosis secondary to an RPE tear, or

⁷ This includes patients who are switched from aflibercept 2mg to aflibercept 8mg and then switched back to aflibercept 2mg following disease recurrence on aflibercept 8mg and a consequent requirement for dosing more frequently than every 8 weeks (which is not supported for aflibercept 8mg – see Section 4.2 for more information).

⁸ According to the licensed posology for aflibercept 8mg, treatment intervals may be extended up to 5 months.

⁹ However, this is subject to clinician discretion and varies with individual patient.

¹⁰ See Appendix 1 for more information.

- atrophy (absence or thinning of RPE and/or retina), or
- cystic degeneration (persistent intra-retinal fluid or tubulations unresponsive to treatment)
- Eye develops severe, progressive loss of VA despite optimal treatment. Defined here as:
 - reduction of BCVA in treated eye to <6/96 on 2–3 consecutive visits, attributable to AMD in the absence of other pathology¹¹, or
 - reduction in BCVA of ≥30 letters in treated eye compared to either baseline and/or best recorded level since baseline, on 2–3 consecutive visits (consider switch if failure to 1 drug)

2.6 Failed treatment extension

After a failed treatment extension, treatment should recommence at the interval received prior to the failed extension.

Disease activity changes over time. Consequently, extending treatment intervals should still be considered despite previous unsuccessful attempts, taking into account patient factors such as vision in the fellow eye. Before re-attempting extension, consider fixing dosing at the last effective treatment interval for 2–3 injections, depending on recurrence severity, or for longer in the case of multiple failed extensions.

¹¹ In eyes with VA of 6/96 or worse, consider anti-VEGF treatment for late AMD (wet active) 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 patients with advanced disease, specialist assessment is required to consider the degree of structural damage and potential benefit from treatment, especially if the patient has excellent vision in the unaffected eye and is unlikely to gain functional benefit.

3 Aflibercept (Eylea and biosimilars) 2mg

3.1 Licensed posology

The licensed posology for aflibercept (Eylea and biosimilars) 2mg in wet AMD is detailed in Box 2.

Box 2 – Licensed posology for aflibercept (Eylea and biosimilars) 2mg in wet AMD

The recommended dose is 2 mg aflibercept (Eylea and biosimilars), equivalent to 0.05 mL.

Aflibercept treatment is initiated with 1 injection per month for 3 consecutive doses. The treatment interval is then extended to 2 months.

Based on the physician's judgement of visual and/or anatomic outcomes, the treatment interval may be maintained at 2 months or further extended using a treat-and-extend dosing regimen, where injection intervals are increased in 2- or 4-weekly increments to maintain stable visual and/or anatomic outcomes. If visual and/or anatomic outcomes deteriorate, the treatment interval should be shortened accordingly.

There is no requirement for monitoring between injections. Based on the physician's judgement the schedule of monitoring visits may be more frequent than the injection visits.

Treatment intervals greater than 4 months or shorter than 4 weeks between injections have not been studied.

3.2 Guidance on use

New patients commencing treatment for wet AMD for whom aflibercept 2mg is to be used should be started on a biosimilar rather than Eylea.

All patients currently receiving Eylea 2mg should be switched to a aflibercept biosimilar unless specific reasons are identified which prevent this (new loading doses are not required).

Treatment with aflibercept 2mg (Eylea and biosimilars) should be commenced with one injection per month for 3 consecutive doses (i.e., day 1, week 4, week 8). The treatment interval is then extended to 2 months¹².

At the 4th visit (week 16) – and at all subsequent injection visits – VA assessment and optical coherence tomography (OCT) imaging should be performed to determine the interval before the next injection, which may be extended, maintained or reduced according to the criteria set out in Figure 1.

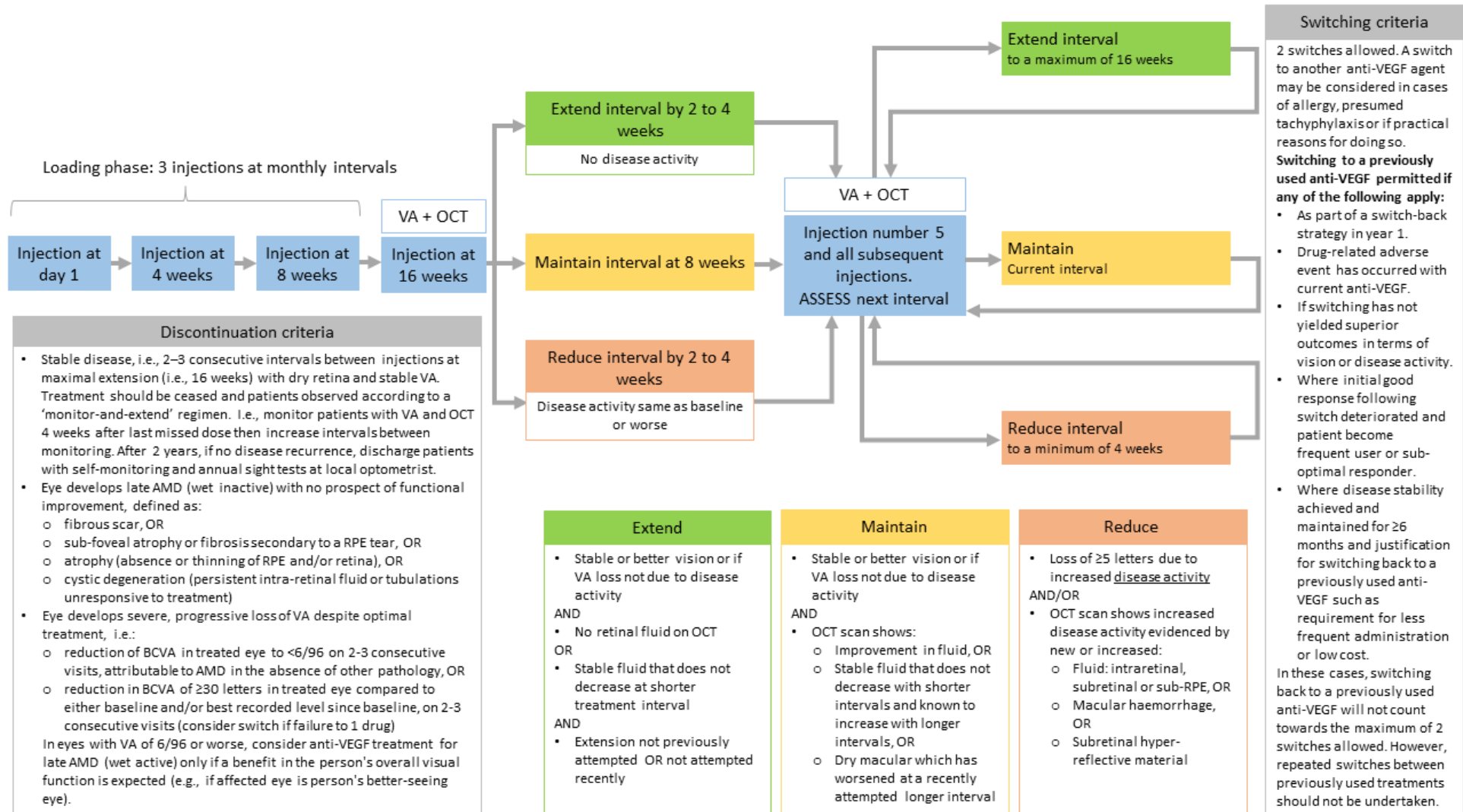
The aim should be to reduce the frequency of injections using a treat-and-extend approach, as clinically appropriate. According to the licensed posology for aflibercept 2mg, the treatment interval may be extended using a treat-and-extend dosing regimen, in 2- to 4-week increments up to a maximum interval of 16 weeks between injections, unless signs of activity or a decrease in VA is

¹² Assessing visual acuity and OCT imaging at baseline and at visit 4 and each subsequent visit is the minimum. If capacity allows, monitoring may also be considered during the loading phase to help guide subsequent adjustments to the dosing interval as part of a treat-and-extend approach. If visual acuity is assessed and OCT imaging undertaken at visit 3 (i.e., week 8) and disease activity is detected, consider maintaining the treatment interval at 4 weeks.

noted. In most cases, 2-week incremental extensions should be considered. In patients with a stable or improved VA and a completely dry macula, 4-week increments may be considered.

If visual and/or anatomic outcomes deteriorate, the treatment interval may be reduced accordingly, to a minimum of 4 weekly. Consider reducing the interval between injections by 2- to 4-week decrements. Once visual and anatomic outcomes are stable, the treatment interval may be increased using a treat-and-extend regimen as described above.

Figure 1 – Aflibercept (Eylea and biosimilars) 2mg pathway for the treatment of wet AMD (adapted from Baily et al., 2023)



4 Aflibercept (Eylea) 8mg

4.1 Licensed posology

The licensed posology for aflibercept 8mg in wet AMD is detailed in Box 3.

Box 3 – Licensed posology for aflibercept 8mg in wet AMD

The recommended dose is 8 mg aflibercept, equivalent to 0.07 mL.

Aflibercept treatment is initiated with 1 injection per month for 3 consecutive doses. Injection intervals may then be extended up to every 4 months based on the physician's judgement of visual and/or anatomic outcomes. Subsequently, the treatment intervals may be further extended up to 5 months, such as with a treat-and-extend dosing regimen, while maintaining stable visual and/or anatomic outcomes. If visual and/or anatomic outcomes deteriorate, the treatment interval should be shortened accordingly based on the physician's discretion.

The shortest interval between 2 injections is 2 months in the maintenance phase.

Aflibercept at monthly doses of 8 mg has not been studied for more than 3 consecutive doses.

The frequency of monitoring visits should be based on the patient's status and at the physician's discretion.

4.2 Guidance on use

Aflibercept 8mg should be administered with caution in people with uncontrolled glaucoma, a significant spike in intraocular pressure (IOP) after injection and in people who have narrow angles (due to larger administration volume).

Treatment with aflibercept 8mg should be commenced with one injection per month for 3 consecutive doses (i.e., day 1, week 4, week 8). The treatment interval is then extended to 2 months.

At the 4th visit (week 16)¹³ – and at all subsequent injection visits – VA assessment and OCT imaging should be performed to determine the interval before the next injection, according to the criteria set out in Figure 2. Maintenance doses of aflibercept 8mg should not be administered more frequently than every 8 weeks.

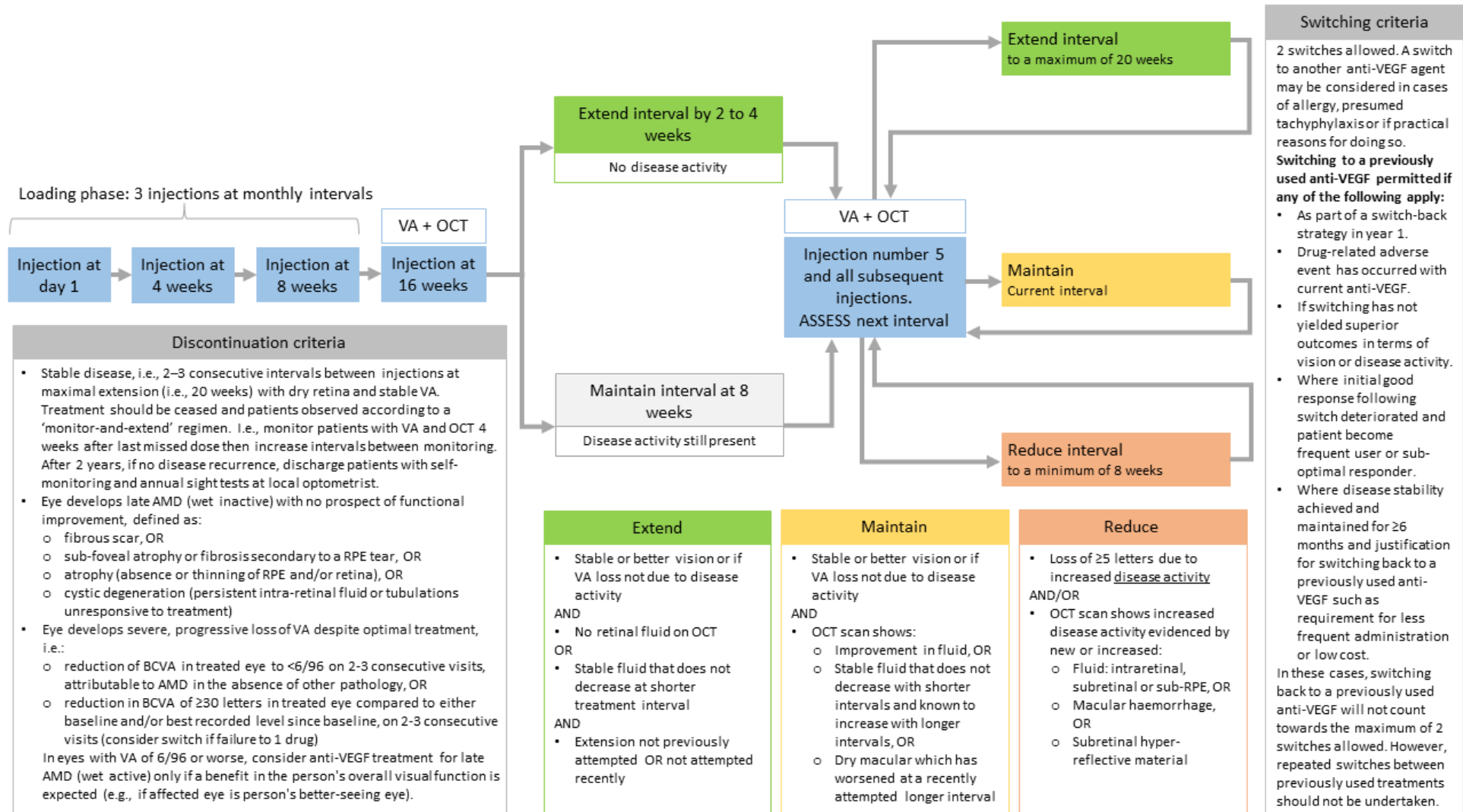
The aim should be to reduce the frequency of injections using a treat-and-extend approach, as clinically appropriate. According to the licensed posology for aflibercept 8mg, the treatment interval may be extended using a treat-and-extend dosing regimen up to a maximum interval of 5 months between injections, unless signs of activity or a decrease in VA is noted. In most cases, 2-week incremental extensions should be considered. In patients with a stable or improved VA and a completely dry macula, 4-week increments may be considered.

If visual and/or anatomic outcomes deteriorate, the treatment interval may be reduced accordingly, to a minimum of 8 weekly. Consider reducing the interval between injections by 2- to 4-week

¹³ Assessing visual acuity and OCT imaging at baseline and at visit 4 and each subsequent visit is the minimum. If capacity allows, monitoring may also be considered at each loading phase injection to help guide subsequent adjustments to the dosing interval as part of a treat-and-extend approach.

decrements. Once visual and anatomic outcomes are stable, the treatment interval may be increased using a treat-and-extend regimen as described above.

Figure 2 – Aflibercept 8mg pathway for the treatment of wet AMD



5 Brolucizumab (Beovu)

5.1 Licensed posology

The licensed posology for brolucizumab in wet AMD is detailed in Box 4.

Box 4 – Licensed posology for brolucizumab in wet AMD

The recommended dose is 6 mg brolucizumab (0.05 ml solution) administered by intravitreal injection every 4 weeks (monthly) for the first 3 doses. A disease activity assessment is suggested 16 weeks (4 months) after treatment start.

Alternatively, 6 mg brolucizumab (0.05 ml solution) may be administered every 6 weeks for the first 2 doses. A disease activity assessment is suggested 12 weeks (3 months) after treatment start. A third dose may be administered based on disease activity as assessed by visual acuity and/or anatomical parameters at week 12.

After the last loading dose, the physician may individualise treatment intervals based on disease activity as assessed by visual acuity and/or anatomical parameters. In patients without disease activity, treatment every 12 weeks (3 months) should be considered. In patients with disease activity, treatment every 8 weeks (2 months) should be considered.

If visual and anatomical outcomes indicate that the patient is not benefiting from continued treatment, brolucizumab should be discontinued.

5.2 Guidance on use

Consideration of brolucizumab as a first line treatment option should be avoided if possible.

Brolucizumab has been associated with potentially serious adverse events (i.e., retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intra-ocular inflammation) that are not commonly associated with intravitreal anti-VEGF agents, and has been the subject of an [MHRA drug safety update](#).

Treatment with brolucizumab should not be considered in patients with a history of uveitis in the treated eye or a history of a systemic disorder associated with uveitis; proceed with caution if only treatable eye.

Brolucizumab should not be commenced in the second eye of a patient until the first eye has received at least 6 months of treatment with brolucizumab without occurrence of serious adverse events including intra-ocular inflammation, retinal vasculitis, retinal vascular occlusion, endophthalmitis and RPE rip.

Based on observational studies, retinal vasculitis and retinal vascular occlusion after brolucizumab treatment appear to be more frequent in female patients and in patients of Japanese ancestry.

All patients should be informed about the risk of vision loss associated with brolucizumab. Consent should include, as a minimum, discussion of the following:

- 4.6% risk of intraocular inflammation (IOI)
- 2.1% risk of irreversible occlusive event

Patients should receive a copy of the consent form with written instructions for symptoms of IOI and an emergency contact number.

At each visit patients on brolucizumab should be asked for the following symptoms:

- Increasing blurring
- New floaters – different to previous floaters
- Pain (except within 24 hrs of injection)
- Sensitivity to bright light
- Redness
- New scotoma – non central

Treatment with brolucizumab should be commenced with one injection per month for 3 consecutive doses (i.e., day 1, week 4, week 8). Optical coherence tomography (OCT) imaging and slit lamp examination should be performed with each loading dose. The treatment interval is then extended to 2 months. According to the [MHRA drug safety update](#), after the first 3 doses (i.e., loading doses), maintenance doses of brolucizumab should not be administered more frequently than every 8 weeks (to reduce the risk of adverse events).

At the 4th visit (week 16) – and at all subsequent injection visits – VA assessment and OCT imaging should be performed to determine the interval before the next injection, which may be extended, maintained or reduced (to a minimum of 8-weekly) according to the criteria set out in Figure 3.

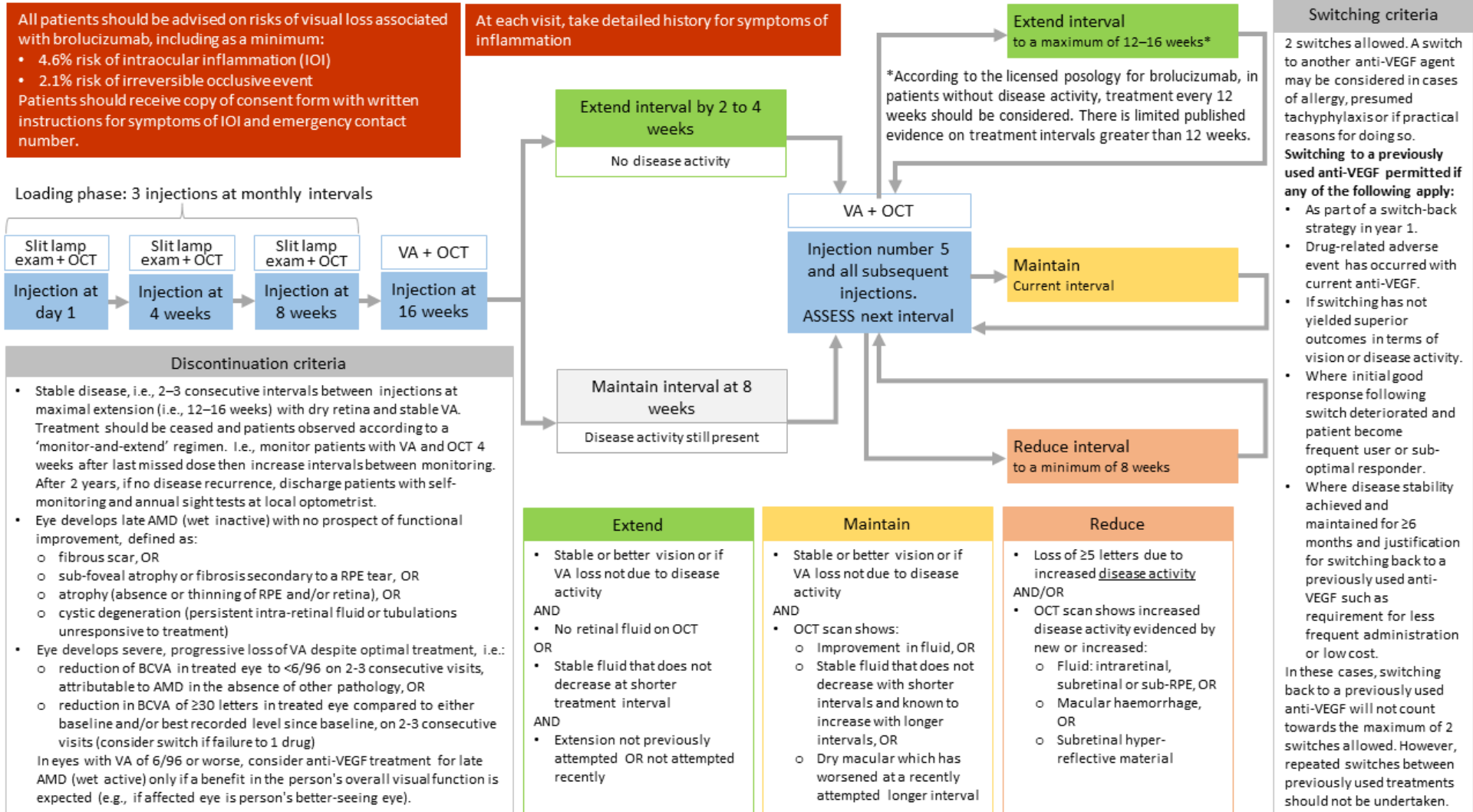
The aim should be to reduce the frequency of injections using a treat-and-extend approach, as clinically appropriate. The treatment interval may be extended by 2 to 4-week increments up to a maximum interval of 12–16 weeks¹⁴ between injections, unless signs of activity or a decrease in VA is noted.

If visual and/or anatomic outcomes deteriorate, the treatment interval may be reduced accordingly, to a minimum of 8 weekly. Consider reducing the interval between injections by 2- to 4-week decrements. Once visual and anatomic outcomes are stable, the treatment interval may be increased as described above.

In patients who develop intraocular inflammation or retinal vascular occlusion, discontinue treatment with brolucizumab and manage events promptly.

¹⁴ According to the licensed posology for brolucizumab, in patients without disease activity, treatment every 12 weeks (3 months) should be considered. There is limited published evidence on treatment intervals greater than 12 weeks.

Figure 3 – Brolucizumab pathway for the treatment of wet AMD



6 Faricimab (Vabysmo)

6.1 Licensed posology

The licensed posology for faricimab in wet AMD is detailed in Box 5.

Box 5 – Licensed posology for faricimab in wet AMD

The recommended dose for faricimab is 6 mg (0.05 mL solution) administered by intravitreal injection every 4 weeks for the first 4 doses.

Thereafter, treatment may be individualised using a treat-and-extend approach following an assessment of the individual patient's anatomic and visual outcomes. The dosing interval may be extended up to every 16 weeks, and extensions in increments of up to 4 weeks should be considered, based on the physician's judgement of the individual patient's anatomic and/or visual outcomes.

If anatomic and/or visual outcomes change, the treatment interval should be adjusted accordingly, and interval reductions of up to 8 weeks may be implemented if deemed necessary. Treatment intervals shorter than 21 days between injections have not been studied*.

For patients on an intravitreal anti-VEGF therapy who are switching to Vabysmo, the treatment regimen may differ from that recommended for treatment-naïve patients. When switching a patient from an intravitreal anti-VEGF therapy to Vabysmo, the length of any subsequent treatment interval is at the discretion of the physician based on the patient's anatomic and/or visual outcomes.

Monitoring between the dosing visits should be scheduled based on the patient's status and at the physician's discretion, but there is no requirement for monthly monitoring between injections.

6.2 Guidance on use

Treatment with faricimab should be commenced with one injection per month for 4 consecutive doses (i.e., day 1, week 4, week 8, week 12).

At the 4th visit (week 12) – and at all subsequent injection visits – VA assessment and optical coherence tomography (OCT) imaging should be performed to determine the interval before the next injection, which may be extended, maintained or reduced (to a minimum of 4-weekly) according to the criteria set out in Figure 4¹⁵.

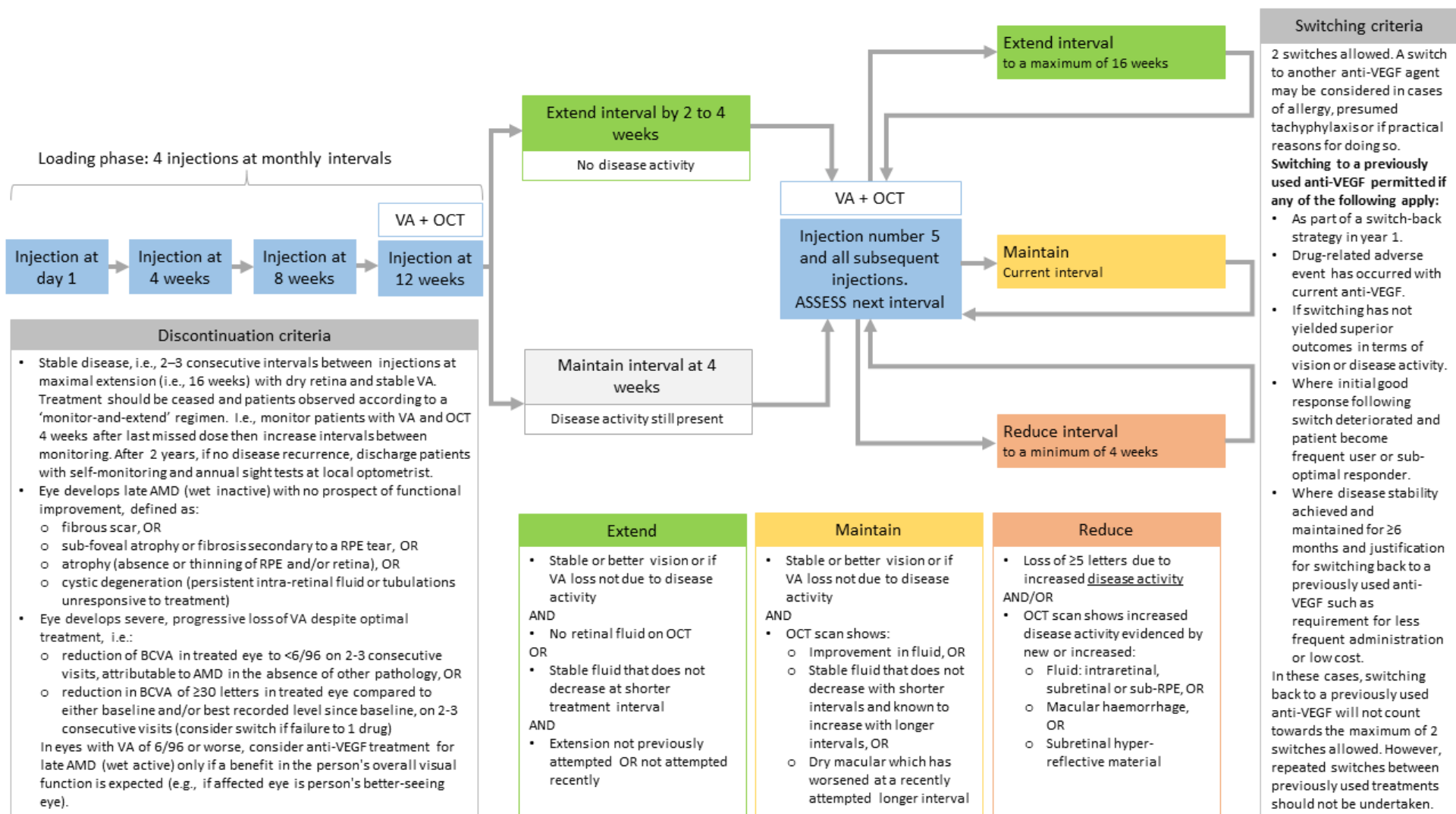
The aim should be to reduce the frequency of injections using a treat-and-extend approach, as clinically appropriate. The treatment interval may be extended using a treat-and-extend dosing regimen in increments of up to 4-weeks, up to a maximum interval of 16 weeks between injections, unless signs of activity or a decrease in VA is noted. In most cases, 2-week incremental extensions should be considered. In patients with a stable or improved VA and a completely dry macula, 4-week increments may be considered.

¹⁵ Assessing visual acuity and OCT imaging at baseline and at visit 4 and each subsequent visit is the minimum. If capacity allows, monitoring may also be considered at each loading phase injection to help guide subsequent adjustments to the dosing interval once the loading phase is completed, as part of a treat-and-extend approach.

*Faricimab off-license dosing: 3 weekly was used in studies to allow flexibility of dose scheduling.

If visual and/or anatomic outcomes deteriorate, the treatment interval may be reduced accordingly, to a minimum of 4 weekly. Consider reducing the interval between injections by 2- to 4-week decrements; interval reductions of up to 8 weeks may be implemented if deemed necessary. Once visual and anatomic outcomes are stable, the treatment interval may be increased using a treat-and-extend regimen as described above.

Figure 4 – Faricimab pathway for the treatment of wet AMD



7 Ranibizumab (Lucentis and biosimilars)

7.1 Licensed posology

The licensed posology for ranibizumab (Lucentis and biosimilars) in wet AMD is detailed in Box 6.

Box 6 – Licensed posology for ranibizumab (Lucentis and biosimilars) in wet AMD

The recommended dose for ranibizumab (Lucentis and biosimilars) in adults is 0.5 mg given as a single intravitreal injection. This corresponds to an injection volume of 0.05 ml. The interval between 2 doses injected into the same eye should be at least 4 weeks.

Treatment in adults is initiated with 1 injection per month until maximum visual acuity is achieved and/or there are no signs of disease activity i.e. no change in visual acuity and in other signs and symptoms of the disease under continued treatment. In patients with wet AMD, initially, 3 or more consecutive, monthly injections may be needed.

Thereafter, monitoring and treatment intervals should be determined by the physician and should be based on disease activity, as assessed by visual acuity and/or anatomical parameters.

If, in the physician's opinion, visual and anatomic parameters indicate that the patient is not benefiting from continued treatment, ranibizumab (Lucentis and biosimilars) should be discontinued.

Monitoring for disease activity may include clinical examination, functional testing or imaging techniques (e.g. optical coherence tomography or fluorescein angiography).

If patients are being treated according to a treat-and-extend regimen, once maximum visual acuity is achieved and/or there are no signs of disease activity, the treatment intervals can be extended stepwise until signs of disease activity or visual impairment recur. The treatment interval should be extended by no more than 2 weeks at a time for wet AMD. If disease activity recurs, the treatment interval should be shortened accordingly.

7.2 Guidance on use

New patients commencing treatment for wet AMD for whom ranibizumab is to be used should be started on a biosimilar rather than Lucentis.

All patients currently receiving Lucentis should be switched to a ranibizumab biosimilar unless specific reasons are identified which prevent this (new loading doses are not required).

Treatment with ranibizumab (Lucentis and biosimilars) should be commenced with one injection per month for 3 consecutive doses (i.e., day 1, week 4, week 8).

At the 4th visit (week 12) – and at all subsequent injection visits – VA assessment and optical coherence tomography (OCT) imaging should be performed to determine the interval before the

next injection, which may be extended, maintained or reduced (to a minimum of 4-weekly) according to the criteria set out in Figure 5^{16, 17}.

The aim should be to reduce the frequency of injections using a treat-and-extend approach, as clinically appropriate. The treatment interval may be extended using a treat-and-extend dosing regimen in 2-week increments up to a maximum interval of 12-16 weeks¹⁸ between injections, unless signs of activity or a decrease in VA is noted.

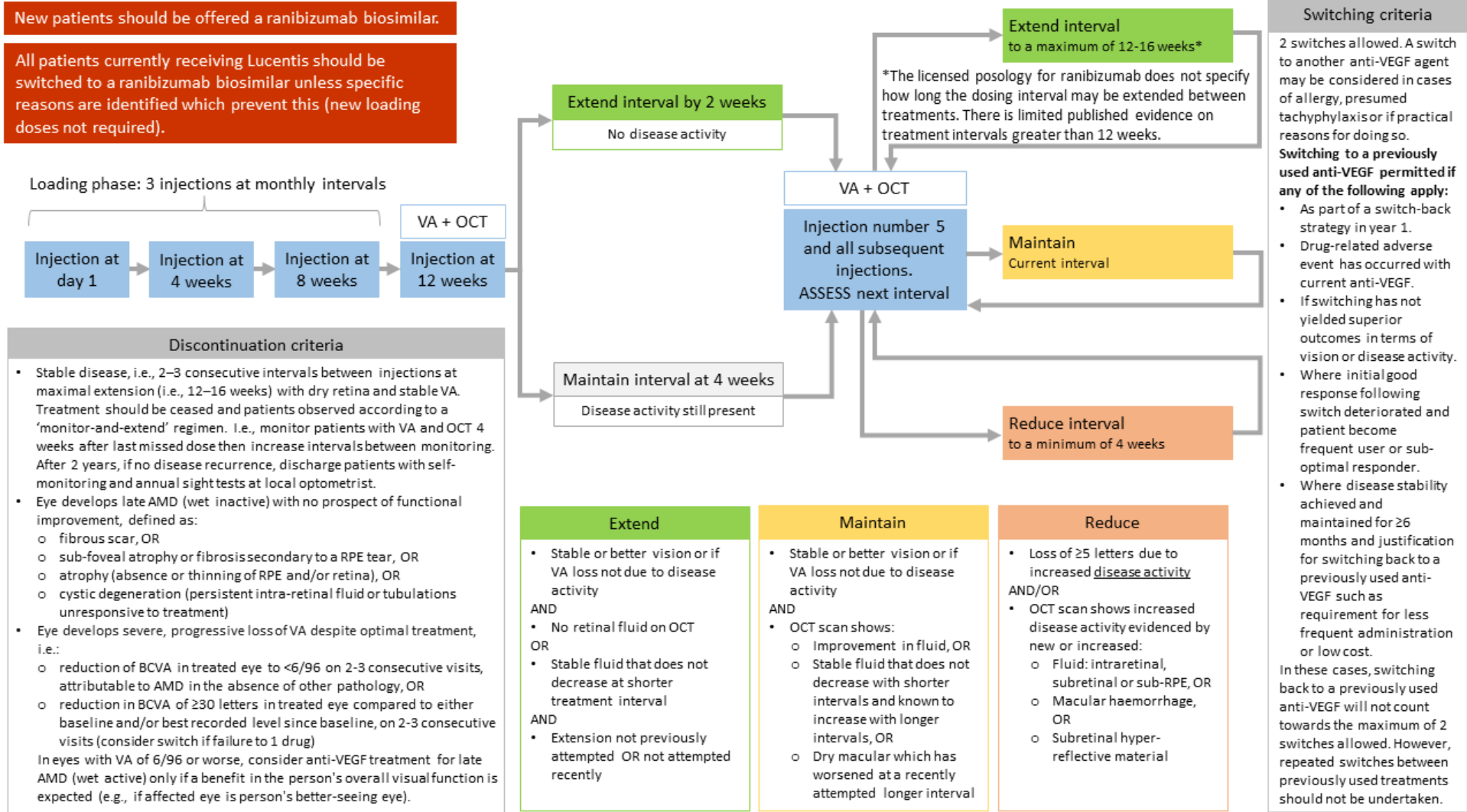
If visual and/or anatomic outcomes deteriorate, the treatment interval may be reduced accordingly, to 4-weekly. Consider reducing the interval between injections by 1- to 2-week decrements. Once visual and anatomic outcomes are stable, the treatment interval may be increased using a treat-and-extend regimen as described above but consider extending by 1-week increments (rather than 2-week increments) where recurrence was associated with retinal fluid.

¹⁶ Assessing visual acuity and OCT imaging at baseline and at visit 4 and each subsequent visit is the minimum. If capacity allows, monitoring may also be considered at each loading phase injection to help guide subsequent adjustments to the dosing interval once the loading phase is completed, as part of a treat-and-extend approach.

¹⁷ Alternatively, if there is a good response, i.e., the patient is dry, they could be offered a PRN treatment plan. If they reactivate, the treat and extend protocol should be administered.

¹⁸ The licensed posology for ranibizumab does not specify how long the dosing interval may be extended between treatments. There is limited published evidence on treatment intervals greater than 12 weeks.

Figure 5 – Ranibizumab (Lucentis and biosimilars) pathway for the treatment of wet AMD



8 References

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Appendix 1 – Classification of AMD

See below for the AMD classification system recommended in NICE guideline 82. The table below also includes terminology commonly used to describe disease progression.

AMD classification	Definition	Commonly used terminology
Normal Eyes	<ul style="list-style-type: none"> No signs of age-related macular degeneration (AMD) Small ('hard') drusen (less than 63 micrometres) only 	No AMD
Early AMD	<p>Low risk of progression:</p> <ul style="list-style-type: none"> medium drusen (63 micrometres or more and less than 125 micrometres), or pigmentary abnormalities <p>Medium risk of progression:</p> <ul style="list-style-type: none"> large drusen (125 micrometres or more), or reticular drusen, or medium drusen with pigmentary abnormalities <p>High risk of progression:</p> <ul style="list-style-type: none"> large drusen (125 micrometres or more) with pigmentary abnormalities, or reticular drusen with pigmentary abnormalities, or vitelliform lesion without significant visual loss (best-corrected acuity better than 6/18), or atrophy smaller than 175 micrometres and not involving the fovea 	<p>Early AMD or age-related maculopathy</p> <p>Intermediate AMD</p>
Late AMD (indeterminate)	<ul style="list-style-type: none"> Retinal pigment epithelial (RPE) degeneration and dysfunction (presence of degenerative AMD changes with subretinal or intraretinal fluid in the absence of neovascularisation) Serous pigment epithelial detachment (PED) without neovascularisation 	
Late AMD (wet active)	<ul style="list-style-type: none"> Classic choroidal neovascularisation (CNV) Occult (fibrovascular PED and serous PED with neovascularisation) Mixed (predominantly or minimally classic CNV with occult CNV) Retinal angiomatous proliferation (RAP) Polypoidal choroidal vasculopathy (PCV) 	Neovascular AMD (nAMD) or wet AMD

AMD classification	Definition	Commonly used terminology
Late AMD (dry)	Geographic atrophy (in the absence of neovascular AMD) Significant visual loss (6/18 or worse) associated with: <ul style="list-style-type: none"> • dense or confluent drusen, or • advanced pigmentary changes and/or atrophy, or • vitelliform lesion 	Advanced dry AMD/ geographic atrophy
Late AMD (wet inactive)*	<ul style="list-style-type: none"> • Fibrous scar • Sub-foveal atrophy or fibrosis secondary to an RPE tear • Atrophy (absence or thinning of RPE and/or retina) • Cystic degeneration (persistent intraretinal fluid or tubulations unresponsive to treatment) Note that eyes may still develop or have a recurrence of late AMD (wet active)	Advanced wet AMD/ disciform scar

* According to NICE guideline 82, late AMD (wet inactive) should not be referred to as 'dry AMD'.