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NHS England

Commissioning Guidance: Medical Retinal Treatment Pathway for Centre-Involving Diabetic Macular Oedema with Visual Impairment

With Herts & West Essex local adaptations (December 2025)

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Hertfordshire and West Essex Integrated Care System

NHS Hertfordshire and West Essex Integrated Care Board

LOCAL ADAPTATION

December 2025 In adopting the NHS England treatment algorithm below, Herts & West Essex Integrated Care System Area Prescribing Committee have agreed the following local adaptations:

DMO with visual impairment but Central retinal thickness (CRT) < 400 microns
This falls below NICE TA treatment threshold and funding for anti-VEGFs has not been agreed for this cohort
[related note 4 in original NHSE document]

Dexamathasone implant frequency and maximum number of treatments
The local commissioning position remains unchanged, with dexamethasone implant being routinely commissioned at approximately 6 monthly intervals (2 implants per year) to a maximum of 7 implants in total (per SmPC).
[related to recommendation 8 in original NHSE document]

Rescue treatments for patients on fluocinolone implant
Rescue treatments (e.g. anti-VEGFs, laser, dexamethasone implant) are not currently locally commissioned for patients on fluocinolone implant.
[related to recommendation 9 in original NHSE document]

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1. Abbreviations

Abbreviation	Explanation
BCVA	Best corrected visual acuity
CRT	Central retinal thickness
CV	Cardiovascular
DMO	Diabetic macular oedema
ETDRS	Early Treatment Diabetic Retinopathy Studies
ICB	Integrated Care Board
IOP	Intraocular pressure
LoE	Loss of exclusivity. Date where generic competitors may enter the market.
MHRA	Medicines and Healthcare Regulatory Agency
NHS	National Health Service
NICE	National Institute of Healthcare and Excellence
NG	NICE Guidance. Recommendations on the appropriate treatment and care of people with specific diseases and conditions within the NHS in England and Wales. Commissioning of medicines recommended in NICE guidance is not mandatory.
NOD	National ophthalmology database
OCT	Optical coherence tomography
PRN	Pro re nata or as required. A treatment regime for treating DMO where medications are given as needed.
RCOphth	The Royal College of Ophthalmologists
SHRM	Subretinal Hyper-reflective Material
SPC	Summary of product characteristics
TA	Technology appraisal. The NHS is legally obliged to fund and resource medicines and other treatments recommended by NICE's technology appraisals
T&E	Treat and extend. A standard treatment regimen for treating DMO, where the interval for the next anti-VEGF injection is extended by 2 to 4 weeks up to a maximum of 24 weeks depending on the anti-VEGF used.
VA	Visual acuity
VEGF	Vascular endothelial growth factor

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2. Definitions

Term	Explanation
Centre-involving diabetic macular oedema	Diabetic macular oedema that involves the central subfield of the Early Treatment Diabetic Retinopathy Studies (ETDRS) grid, which has a diameter of 1 mm. Centre-involving diabetic macular oedema is always clinically significant.
Epiretinal membrane	A condition where a very thin layer of scar tissue forms on the surface of the retina, most importantly at the macula where the vision is sharpest.
Fellow eye	The other eye of 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 an additional 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.
Resolved macular oedema	NICE NG242 defined this as presence of isolated or sparse, small, intraretinal cysts with no other features as seen from optical coherence tomography (OCT) scans.

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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 (T&E) protocol	A standard treatment regimen for treating DMO, where the interval for the next anti-VEGF injection is extended by 2 to 4 weeks up to a maximum of 24 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.
Visual impairment	NICE NG242 defined this as 78 ETDRS letters or less, or a Snellen acuity of 6/9 or worse, or logMAR 0.2 or worse. There is no mandatory visual acuity threshold to access treatment under NICE TAs.
Vitreomacular traction	A condition where there is an unusually strong attachment between the vitreous gel and the very centre of the retina. The central retina is therefore lifted up slightly and does not function properly, resulting in reduced and distorted central vision.
Worse-seeing eye	Also known as the weaker eye. This occurs when one eye sees significantly worse than the other eye.

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3. Treatment algorithm for centre-involving diabetic macular oedema with visual impairment

If more than one treatment is suitable, use the best value treatment and best value brand available locally through national procurement framework. **PRESCRIBE BY BRAND.**

Does the patient have visual impairment?

NO → Macular laser or observation. Refer to NG242 for details

YES

Is NICE TA criteria met:
Central retinal thickness (CRT) ≥ 400 microns

NO → **NICE criteria do not apply – Pathway not applicable**

YES

Treatment options (see Note 4)

	Anti-VEGFs suitable	Anti-VEGFs not suitable
1st choice	**Aflibercept 2mg** (TA346) switch to biosimilar when available OR **Ranibizumab biosimilar** (TA274)	**Dexamethasone intravitreal implant** (TA824) *normally used to test for steroid responsiveness*
2nd choice	**Aflibercept 8mg** OR **Faricimab** (TA799)	**Fluocinolone intravitreal implant** (TA953)
3rd choice	**Brolucizumab** (TA820)	

Is there evidence of response to treatment?
Assess response based on visual acuity and disease activity (including CRT).
For **anti-VEGFs**: Check delivery of injections. See Figure 1 for details. First review after loading dose completed (3-6 months after first injection).
For **steroids:** Monitoring intervals determined by clinician. Review before next dose.

YES → **Anti-VEGFs:** Continue treatment, tailor regime (T&E/ regular/ PRN) according to patient (see Table 5)
Steroids: Continue treatment (see Table 6)

Ongoing monitoring intervals will be determined by clinician, depending on treatment type, treatment regime and disease activity.

The management of the patient should be reviewed by a senior clinician **post-loading** and **annually** to consider if continuation of treatment is in patient's best interest.

NO – switch to alternative preparation

SWITCH treatment if (see Note 6):
- Suboptimal or poor response
- Adverse drug reaction
- Treatment burden (e.g. unable to safely extend treatment intervals >7 weeks OR anti-VEGF treatment frequency not acceptable to patient)

Second-choice anti-VEGFs may be considered first-line for the following reasons (see Note 4):
- Capacity constraints
  - Note this may not be cost-effective in the long-term and needs to be agreed locally with commissioners
- Patient factors
- Clinical factors

At any point of treatment, consider STOPPING (see Note 8) if:
- VA <25 letters attributed to DMO **OR**
- No response (i.e. no change or worsening CRT AND VA) **OR**
- Irreversible structural changes WITH no prospect of visual improvement with continued treatment

Scenarios where steroid implants may be more appropriate:
- Recent (within 6 months) CV events
- Pregnancy (if benefits outweigh risks- use dexamethasone due to shorter half-life)
- Unable to comply with frequent anti-VEGF injections

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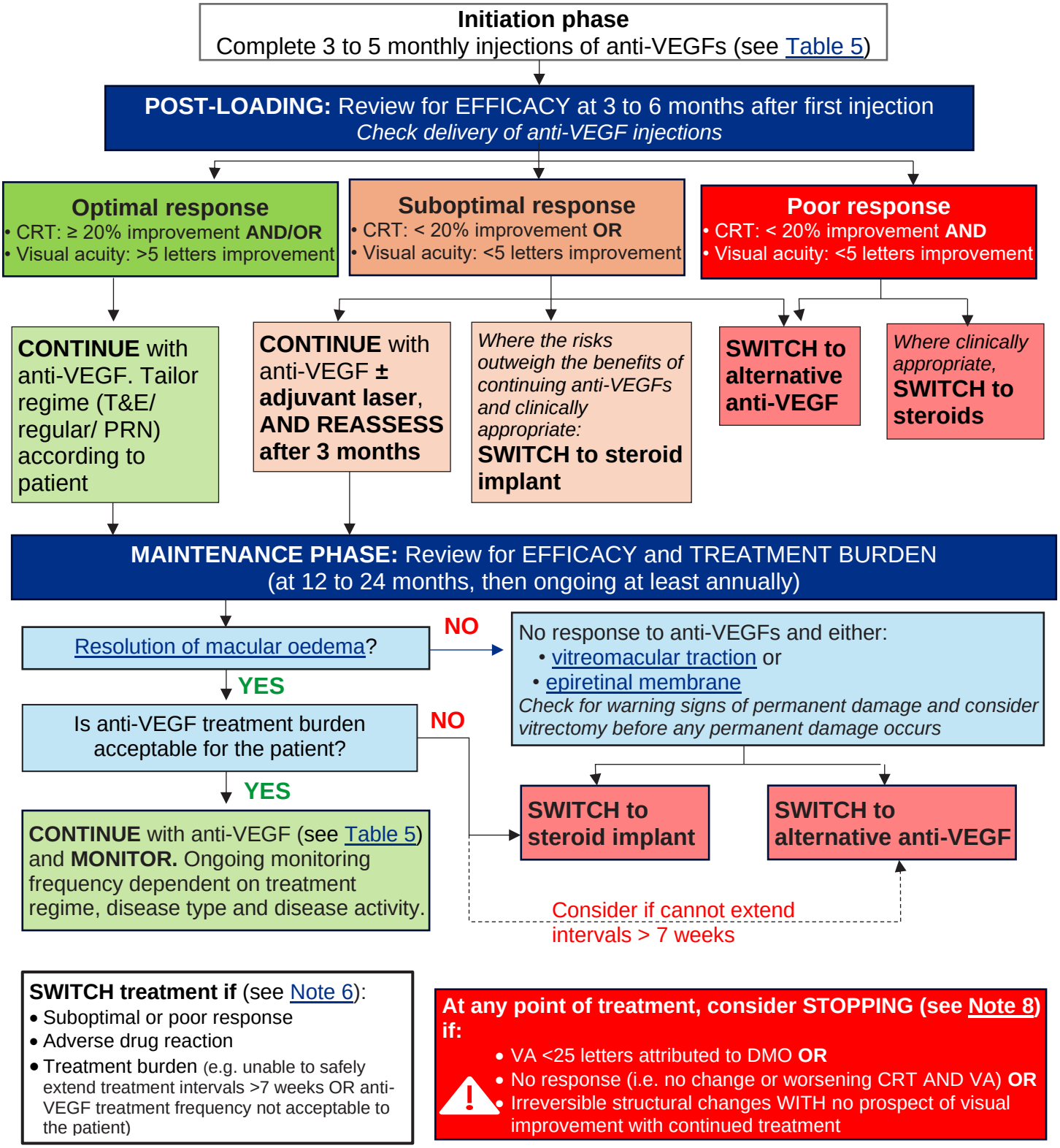
Figure 1. Recommended anti-VEGF efficacy and treatment burden check time points (see Note 5, Note 6 and Note 7)



SWITCH treatment if (see Note 6):

- Suboptimal or poor response
- Adverse drug reaction
- Treatment burden (e.g. unable to safely extend treatment intervals >7 weeks OR anti-VEGF treatment frequency not acceptable to the patient)

At any point of treatment, consider STOPPING (see Note 8) if:

- VA <25 letters attributed to DMO **OR**
- No response (i.e. no change or worsening CRT AND VA) **OR**
- Irreversible structural changes WITH no prospect of visual improvement with continued treatment

Anti-VEGFs- additional information (see Note 6)

If there is no clinical benefit after **THREE** months post-switching to an alternative anti-VEGF, consider **SWITCH BACK** to previous anti-VEGF it is more cost-effective.

Consider switching to an **alternative anti-VEGF** or **steroid implant** if this is the patient's second anti-VEGF, where clinically indicated.

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Table 5. Anti-VEGF dosing details according to SPC

General information for all anti-VEGFs:
Based on the physician's judgement of visual and/or anatomic outcomes, **the treatment intervals can be increased** to maintain stable visual and/or anatomic outcomes.
If visual and/or anatomic outcomes deteriorate, the **treatment interval should be shortened** accordingly.

Anti-VEGF	Loading dose	Maintenance dose (post-loading, with disease activity)	Treat-and-extend dose increment intervals (maximum treatment intervals)	Minimum dose intervals
First choice				
Aflibercept 2mg (TA346) (switch to biosimilars once available)	2mg monthly for 5 months	1 injection every 2 months	2 weeks (up to 1 injection/ 16 weeks)	4 weeks
Ranibizumab biosimilar (TA274)	0.5mg every 4 weeks for 3 months or more until maximum visual acuity achieved	4 weekly	Up to 4 weeks (no specific maximum treatment intervals specified in SPC)	4 weeks
Second choice				
Aflibercept 8mg	8mg monthly for 3 months	1 injection every 2 months	Not specified (up to 1 injection/ 16 weeks, can be further extended to 1 injection/ 24 weeks)	8 weeks*
Faricimab (TA799)	6mg every 4 weeks for 3 doses	1 injection every 8 to 16 weeks	Up to 4 weeks (up to 1 injection/ 16 weeks)	4 weeks**
Third choice				
Brolucizumab (TA820)	6mg every 6 weeks for 5 doses	Without disease activity: 1 injection every 12 weeks With disease activity 1 injection every 8 weeks	Not specified (up to 1 injection/ 16 weeks) Extension should only happen after 12 months of treatment	8 weeks

Off-license dosing details
*Aflibercept 8mg off-license dosing: max 4 weekly for 3 consecutive doses were used in studies.
**Faricimab off-license dosing: 3 weekly was used in studies to allow flexibility of dose scheduling.[10,11]
The safety and efficacy of off-license dosing has not been evaluated. Therefore, NHS England do not recommend routine commissioning of off-license dosing.

For patients with baseline ETDRS < 69 letters, Protocol T study demonstrated efficacy hierarchy for the following drugs: aflibercept (most efficacious) > ranibizumab > bevacizumab (least efficacious).[1210] There is lack of evidence which directly compares the efficacy hierarchy for all anti-VEGFs which have UK marketing authorisation.

Figure 2. Indicative anti-VEGF combined costs (drug and activity) based on average number of doses from NHSE modelling and real-world NHS data at the time of writing

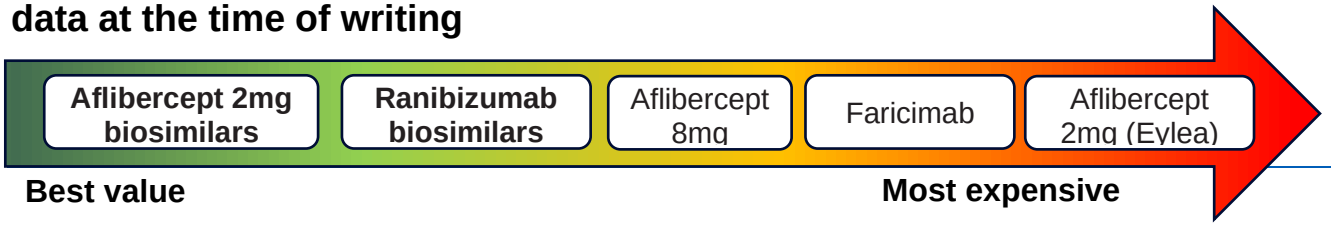

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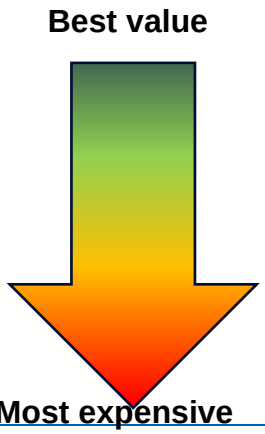
Table 6. Steroid implant dosing details according to SPC

Intravitreal steroid implant	Dose	Other notes
Preferred choice: Dexamethasone (TA824)	700 micrograms (one implant) intravitreally into the affected eye. Manufacturer recommends retreatment may be performed after approximately 6 months if the patient experiences decreased vision and/or an increase in retinal thickness, secondary to recurrent or worsening diabetic macular oedema.	Administration to both eyes concurrently is not recommended. Common clinical practice is to administer one eye at a time for the first injection to review for response and side effects. If no concerns and clinically appropriate, clinicians may choose to administer both eyes at the same time. Manufacturer reports no experience of the efficacy or safety of repeat administrations in DMO beyond 7 implants.
Fluocinolone (TA953)	190 micrograms (one implant) intravitreally into the affected eye. An additional implant may be administered after 12 months if the patient experiences decreased vision or an increase in retinal thickness secondary to recurrent or worsening diabetic macular oedema.	Retreatments should not be administered unless the potential benefits outweigh the risks. Only patients who have been insufficiently responsive to prior treatment with laser photocoagulation or other available therapies for diabetic macular oedema should be treated with fluocinolone. The safety and efficacy of fluocinolone administered to both eyes concurrently has not been studied. It is recommended that an implant is not administered to both eyes at the same visit. Subject to local commissioning, up to 2 implants per eye is recommended to be commissioned.

Figure 3. Indicative combined costs (drug and activity) of anti-VEGFs and steroid implants based on average number of doses from NHSE modelling and real-world NHS data at the time of writing



Aflibercept 2mg biosimilars (best value)
Ranibizumab biosimilars (best value)
Aflibercept 8mg
Faricimab
Dexamethasone implant (6 monthly/ 2 implants per year)
Fluocinolone implant (1 implant over 3 years)
Aflibercept 2mg (Eylea)
Fluocinolone implant (2 implants over 3 years)

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Table 7. Estimated Loss of Exclusivity (LoE)[16]

Drug	Estimated LoE
Ranibizumab	July 2022
Aflibercept 2mg	End of November 2025
Aflibercept 8mg	2039
Faricimab	2037
Brolucizumab	2034
Dexamethasone implant	2026 (no planned generics launch at the time of writing)
Fluocinolone acetonide implant	Expired- pending on regulatory approval of generics

Note: Patents can be liable to legal challenge and dates may change. Some medicines may be subject to additional patents on, for example, therapeutic use or device.

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4. Notes

Note 1: Treatment goals

- Improvement (> 5 letters) or stabilisation of visual acuity (NICE NG242) [1]
- Improvement in central retinal thickness (NICE NG242) [1]
- Manageable treatment burden for the patient

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:

Recommendation 1. 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.

Rationale

Communicating with patients at the beginning of treatment about all treatment possibilities is crucial for setting realistic expectations. This transparency helps patients understand the potential outcomes, benefits, and risks associated with each option, enabling them to make informed decisions about their care.

Clear communication can help mitigate anxiety and prevent misunderstandings or disappointments later on, ensuring that patients have a clear and accurate understanding of their treatment journey from the outset.

Patients can be signposted to the Macular Society for clear, patient-friendly information on diagnosis, treatment options, and support services (see link below).
https://www.macularsociety.org/macular-disease/macular-conditions/diabetic-macular-oedema/

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Note 2: Supporting diabetic management in eye care (NICE NG242)[1]

Effective diabetes management is essential to reduce the risk of progression of eye disease. Patient should be encouraged to improve glycaemic and blood pressure control.
All clinicians involved in the caring of people with DMO should work collaboratively to ensure good glycaemic and blood pressure control in diabetic patients.
For full guidance, refer to NICE NG242, Section 1.1: Managing diabetes to support best eye care.

Note 3: 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'*.[2]
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 4: Choice of therapy

Choice of treatment between anti-VEGFs or steroid implants will need to consider risk of IOP, cardiovascular risk, cataract formation and injection frequency. [1] If more than one treatment option is suitable and service capacity allows for timely treatment, choose the best-value medicine (taking into account administration costs, frequency and commercial arrangements) unless an order of preference is stated in the TAs or by the local commissioner.

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.[17] If more than one biosimilar brand is available, choose best value brand available locally.

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Recommendations for best practice:

Recommendation 3. Where clinically appropriate, use anti-VEGFs first.
First choice options: Aflibercept 2mg (TA346)- switch to biosimilar once available OR ranibizumab biosimilar (TA274)

Rationale:

- Using confidential price discounts, ranibizumab biosimilar (Ongavia®) and brolucizumab had ICERs below £20,000 per QALY, while aflibercept 2mg, ranibizumab originator and faricimab had ICERs below £25,000 per QALY, compared to no treatment. Bevacizumab was the most cost-effective anti-VEGF treatment due to its significantly lower cost.[18] It is expected that aflibercept 2mg biosimilars would have similar ICERs as ranibizumab biosimilar (below £20,000 per QALY). Therefore, ranibizumab biosimilar and aflibercept 2mg biosimilar are best value options compared to other anti-VEGFs.
- Brolucizumab is not recommended as a first choice option due to concerns due to intraocular inflammation concerns (see 2022 MHRA alert).[19] The use of bevacizumab for this population is not licensed in the UK and would be considered off-label. The expert working group have excluded bevacizumab in the recommendations because other licensed options are available.
- At the time of writing, branded aflibercept 2mg is one of the more expensive options but there are opportunity savings to be made once aflibercept 2mg biosimilars become available (loss of exclusivity expected end of November 2025).

Recommendation 4. Use aflibercept 8mg OR faricimab (TA799) as second choice anti-VEGF options. This is usually when high injection frequency is not acceptable with first choice options.

Rationale:

- More expensive than aflibercept 2mg biosimilar and ranibizumab biosimilar (taking into account administration frequency and drug cost per annum) according to NHSE modelling. Faricimab has a higher ICER (below £25,000 per QALY) compared to ranibizumab biosimilar (below £20,000 per QALY). It is expected that the ICER for

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aflibercept 8mg would be similar to faricimab. Both aflibercept 8mg and faricimab have the same number of injections based on NHSE modelling. Aflibercept 8mg is the best value option based on current prices.

- Using second-choice options as first line treatments is not a cost-effective, long-term approach. Based on NHSE modelling, the average difference in required annual injections in the first 3 years (monotherapy) between aflibercept 2mg (4.6 injections per year) and faricimab/ aflibercept 8mg (4 injections per year) is relatively small. In single switch and double switch pathways, the number of appointments per patient over 3 years required is **broadly similar across treatment options**, with **faricimab and aflibercept 8mg** associated with **slightly fewer appointments** (see implementation through NHS commissioning and contracting systems for details).
- For a small number of patients, second-choice options may be used as a first-line treatment if appropriate.
- Examples where use may be appropriate:
    - Capacity constraints
        - Capacity constraints are normally represented by an inability within a service to deliver treatment in a timely way to patients as part of business as usual (BAU). This could be represented by frequent insourcing and outsourcing in order to meet intravitreal treatment demand. Definition of capacity constraints needs to be agreed locally between providers with commissioners.
        - Providers 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. There are examples available where Trusts have managed their waiting lists and used transformation approaches whilst still using better-value treatment options.
    - Patient factors
        - The following patient groups may be better managed with the least number of injections which will outweigh the cost. These are people with or requiring:
            - learning difficulties
            - dementia
            - hospital transport

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

- Clinical factors
  - Non-responder to first-choice drugs in fellow eye previously
  - Treatment harmonisation (see recommendation 6 below)

Recommendation 5. Use brolucizumab (TA820) as a third-choice anti-VEGF option.

Rationale:

- Risk of intraocular inflammation with brolucizumab.[9] See also 2022 MHRA alert.[19]

Recommendation 6. Where one eye is already on **an anti-VEGF**, but the other eye qualifies for another treatment, prioritise treatment harmonisation by choosing the best **anti-VEGF** treatment option for both eyes (i.e using only one drug for both eyes).

Rationale:

- To minimise drug administration error
- Allows easy identification of adverse drug reactions of a single drug compared to administering two different drugs.

Recommendation 7. If the patient's condition has not responded well enough to, or if they cannot have non-corticosteroid therapy, use steroid implants.
First choice: dexamethasone implant (NICE TA824)
Second choice: fluocinolone implant (NICE TA953)

Rationale:

NICE TA824 recommends dexamethasone intravitreal implant an option for treating visual impairment caused by diabetic macular oedema in adults only if their condition has not responded well enough to, or if they cannot have non-corticosteroid therapy. Fluocinolone acetate implant is recommended in NICE TA953 as an option for treating visual impairment

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caused by chronic diabetic macular oedema that has not responded well enough to available treatments in adults.

Based on NHSE modelling data, dexamethasone implant (6-monthly) is the better value option than fluocinolone implant (taking into account administration costs, frequency and drug cost per annum). Approximately 40% patients on fluocinolone may need rescue treatments (e.g. anti-VEGFs, dexamethasone implant) which may make it less value compared to dexamethasone implant (FAME study and IRISS registry study).[14,15] This extra cost could not be modelled because it would be dependent on the frequency and type of rescue treatments used. To account for the potential additional costs involved, NHSE has recommended fluocinolone as a second-choice option.

Note 5: Monitoring recommendations

Recommendation 8. For anti-VEGFs, consider efficacy assessment post-loading (typically around 3-6 months) and a change in therapy if suboptimal response.

Rationale:

This time point was chosen because Protocol I data has shown that anatomical and functional response assessment at week 12 could help identify patients who are likely to receive continued benefit from anti-VEGFs earlier.[21,23] Eyes with a poor anatomical response (i.e. CRT reduction < 20%) at 3 months were less likely to achieve a strong anatomical response (i.e. ≥20% CRT reduction) at year 1.[21] Eyes with early suboptimal functional response (i.e. < 5 letter ETDRS improvement) continued to have suboptimal functional response (53%) after 3 years of treatment.[22]

Some patients may have a delayed response to anti-VEGFs and may benefit from delayed switching at 12 months to minimise the adverse events risks with steroids (NICE NG242).[1] However, this would be uncertain and slow.[23] Given that patients with DMO normally have multiple co-morbidities and with high treatment burden not necessarily related to DMO, it is critical to identify those who were least likely to benefit from further treatment and change treatment earlier to avoid further vision loss.

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The expert working group recognised the risk of adverse drug reactions associated with early switching to steroids. Therefore, patients should only switch from anti-VEGFs to steroids if the risks outweigh the benefits of continued anti-VEGF treatment.

Recommendation 9. Consider using the following criteria to define response:

Optimal response

- CRT: ≥ 20% improvement AND
- Visual acuity: > 5 letters improvement

Suboptimal response

- CRT: < 20% improvement OR
- Visual acuity: ≤ 5 letters improvement

Poor response

- CRT: < 20% improvement AND
- Visual acuity: ≤ 5 letters improvement

Rationale:

NICE NG242 defined suboptimal response as:[1]

- Reduced vision as a result of diabetic macular oedema OR
- Increased diabetic macular oedema OR
- No change or increase in retinal thickness related to diabetic macular oedema

In clinical practice, patients who do not have an optimal response may not fit into the criteria defined by NICE. More defined criteria are recommended by the expert working group to identify suboptimal/ poor responders early, with consideration to either optimise or switch therapy.

CRT and vision criteria were derived from Protocol I and studies which examined continued anti-VEGF treatment versus early switch to dexamethasone.[21,22,24,25]

Recommendation 10. For anti-VEGFs, consider treatment burden and efficacy assessment at 12 to 24 months from the start of treatment. See Note 6 if treatment switch to steroid implants or alternative anti-VEGF is indicated.

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Rationale:

NICE NG282 recommends an evaluation at 12 months.[1] Clinical experts indicated that some patients may take longer to respond and benefit from an additional assessment at 24 months from the start of treatment. To cover both scenarios, the expert working group recommends a time range (12 to 24 months) for assessment.

Recommendation 11. The management of the patient should be reviewed by a senior specialist annually to consider if continuation of treatment is in patient's best interest.

Recommendation 12. For steroid implants, monitor for raised IOP (which peaks at day 60) and formation or progression of cataract. Monitoring intervals would be determined by the clinician based on individual patient's response and disease activity.

Note 6: Treatment switch considerations

Recommendation 13. Switch to **alternative drug class** if:

- Poor response, defined as:
  - Visual acuity: < 5 letters improvement or worsening
  - Anatomical changes: < 20% improvement in CRT
- Adverse events whilst on therapy. Notable adverse events for treatment class include:
  - Anti-VEGFs: cardiovascular events
  - Steroid implants: raised intraocular pressure

Rationale:

Different mode of actions may aid in resolution of macular oedema. In some cases, same class treatment switch may be more appropriate (see recommendations 18 and 22).

For anti-VEGFs, there is limited safety data in patients with prior history of stroke or transient ischaemic attacks or myocardial infarction within the last 6 months.[9]

Recommendation 14. If patients are switched from an anti-VEGF to a steroid implant, monitor patients for neovascularisation.

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Rationale:

Clinical experts indicated that steroids are less effective in suppressing new vessel growth when compared to anti-VEGFs.

Recommendation 15. Switch from **anti-VEGFs** to **steroid implant** where clinically appropriate, if:

- Frequent injections required to maintain disease stability and anti-VEGF treatment burden is not acceptable to patient
- Pregnancy, provided the benefits of treatment outweigh the risk

Rationale:

- Anti-VEGFs are not recommended for use in pregnancy because it is potentially teratogenic and embryo-/ foetotoxic.[9] Dexamethasone implants may be used (shorter half-life compared to fluocinolone implant), provided the benefits of treatment outweighs the risk.

Recommendation 16. Switch from an **anti-VEGFs** to alternative **anti-VEGF, only if anti-VEGF is still appropriate and**:

- Frequent injections (e.g. inability to safely extend treatment intervals > 7 weeks) are required to maintain disease stability **AND** anti-VEGF treatment is still appropriate **AND** treatment burden not acceptable to either patient or service delivery
- Poor response after completing loading or during maintenance phase
- Adverse drug reaction

Rationale

The cut off treatment interval to switch treatments has been extensively discussed in the expert working group. The expert working group agreed to follow the May 2024 RCOphth wet age-related macular degeneration guidance, which sets the switch threshold at seven weeks.[26]

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There is limited evidence for sequential use of anti-VEGFs in DMO[27,28], but clinical experts have indicated that it would be reasonable to use alternative anti-VEGFs where clinically appropriate to avoid the risks of adverse events with steroid implants.

Recommendation 17. If there is no clinical benefit after **THREE months** post-switching to an **alternative anti-VEGF,** consider switching back to previous anti-VEGF it is more cost-effective. Consider switching to an alternative anti-VEGF or steroids where clinically indicated.

Rationale:

The three-month trial limit is based on consensus from the expert working group to ensure best value medicines are used appropriately in the patient's treatment journey.

Recommendation 18. A limit on the number of different anti-VEGFs which should be commissioned in DMO is currently not stipulated. The expectation is that the first anti-VEGF used should normally be first choice options.

Rationale:

The working group did not make recommendations on the maximum number of commissioned anti-VEGFs due to the adverse reaction risks with steroid implants. This recommendation was made to encourage biosimilars use. Biosimilars are available for ranibizumab and anticipated for aflibercept 2mg by end of November 2025. The working group recognise that some patients may need to remain on originator brand for safety reasons, therefore ranibizumab biosimilars and aflibercept 2mg were specified in our recommendations for sequential anti-VEGF use.

Recommendation 19. Consider **switchback** from **steroid implant** to **anti-VEGFs** if:

- Initial reason for switch was due to the following:
    - cardiovascular events which has been resolved
    - high injection burden
    - vitrectomy
    - anti-VEGF being deemed unsuitable (e.g. due to other co-morbidities requiring frequent hospital appointments)

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AND EITHER

- Patient had a better response (disease activity/ treatment interval/ functional outcome) whilst on anti-VEGF compared to steroid implant **OR**
- Adverse events (e.g. raised intraocular pressure, normally peaks at 60 days post dexamethasone implant).

It is recommended that patients are allowed to trial a different anti-VEGF if the original reason for switch was due to high injection burden.

Recommendation 20. Consider switching from dexamethasone intravitreal implant to fluocinolone intravitreal implant if:

- Therapeutic effects of dexamethasone intravitreal implant lasts < 6 months, requiring frequent retreatment

(see also Note 4)

Note 7: 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
- following cataract surgery, patients may experience worsening visually significant DMO in the early post-operative phase[29]

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Note 8: Stopping treatment (e.g. permanent discontinuation)

Recommendation 23. REVIEW with consideration to stop treatment if, despite optimum treatment:

- visual acuity < 25 letters attributable to DMO in the absence of other pathology (see also Note 7)

  OR

- no response to treatment, defined as:
  - no change or worsening CRT AND
  - no change or worsening visual acuity

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 (for anti-VEGFs only)?
- 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 and there is no potential for further improvement?
- Is the treated eye the WORSE seeing eye?
- Does the patient agree that they DO NOT receive continuing benefits from treatment?

Recommendation 22. Treatment STOP recommended if, despite optimum treatment:

- visual acuity < 15 letters attributable to DMO in the absence of other pathology (see also Note 7)

  OR

- there are irreversible structural changes WITH no prospect of visual improvement with continued treatment.

Rationale:

The above cut off points for visual acuity were based on collective expert opinion from the expert working group. The working group cannot define the number of treatments which is deemed "reasonable" because this would be patient-specific. NICE NG242 did not make

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recommendations on the clinical features which might indicate the need to stop treatment due to lack of evidence.[1]

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.

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