NHS
South West London

South West London
Diabetic Macular Oedema (DMO) Drug Pathway
Version 3.1

Contents:

Local Adaptation:

In adopting the NHS England Commissioning Guidance: Medical Retinal Treatment Pathway for Centre-Involving Diabetic Macular Oedema with Visual Impairment, South West London Integrated Commissioning Board (SWL ICB) have agreed the following local adaptations:

1. **Second choice treatment options**
   - Aflibercept 8mg is the preferred second choice option over faricimab.
   - For a small number of patients meeting specified patient or clinical factors, second choice options can be used first. There is no agreement between providers and SWL ICB for first line use of second choice options due to capacity constraints.
2. **DMO and Central Retinal Thickness (CRT) less than 400 microns**
   For patients with CRT<400, treatment with anti-VEGFs biosimilars (aflibercept 2mg biosimilar OR ranibizumab biosimilar only) is recommended in the national guidance but commissioning is not mandated. This is currently not commissioned in SWL and will need further consideration, including factors such as patient numbers and cost impact, before proposing it as a service development.
3. **Rescue Treatments**
   Rescue treatments (e.g. anti-VEGFs, dexamethasone implant) for patients on fluocinolone implant is not currently commissioned in SWL and commissioning is subject to local decision. This will need further consideration, including factors such as patient numbers and cost impact, before proposing it as a service development.
4. **Visual acuity < 25 letters OR no response**
   SWL do not commission aflibercept 8mg, faricimab, or brolucizumab for patients with visual acuity < 25 letters in the absence of other pathology AND no response (defined as no change or worsening CRT AND no change or worsening visual acuity) despite optimum treatment. If following review, it is decided that treatment should continue, use first line biosimilars (aflibercept biosimilar 2mg or ranibizumab biosimilar) and stop treatment if, despite optimum treatment:
   - visual acuity < 15 letters attributable to DMO in the absence of other pathology OR
   - there are irreversible structural changes no prospect of visual improvement with continued treatment.

Version number	Main amendments	Approval date
0	Refer to previous version control	22 Jul 2015
1.0	Refer to previous version control	15 Dec 2021
2.0	Refer to previous version control	20 Mar 2024
2.1	Refer to previous version control	12 April 2024
3.0	Adoption of NHSE Commissioning Guidance: Medical Retinal Treatment Pathway for Centre-Involving Diabetic Macular Oedema with Visual Impairment (version 1.0).	28 Nov 2025
3.1	Updated to include 'Background' and 'Key recommendations' sections present in the final NHSE version 1.0. Change in wording from 'OR' to 'AND' in Recommendation 4.	18 Feb 2026
Date of next review: 3 years (or earlier if indicated)		

Approved by: SWL Integrated Medicines Optimisation Committee **Date:** 18th February 2026

NHS England

Commissioning Guidance: Medical Retinal Treatment Pathway for Centre-Involving Diabetic Macular Oedema with Visual Impairment v1.0

Publication Date: 17/10/2025 Version 1.0

Table of Contents

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

2. Background

Diabetic macular oedema (DMO) is the most common cause for sight loss in people with diabetes.[1] Almost 4.6 million people were diagnosed with diabetes in England in 2023/24, and the condition is more common in people of African-Caribbean and South Asian family origin than in those of European family origin.[2] Approximately 7% of people with diabetes may have DMO in England, of whom 39% have clinically significant macular oedema (CSMO).[3]

Good management of diabetes and other risk factors may delay the onset and progression of DMO. This includes diet and lifestyle modification, blood pressure control and pharmacological treatments. For DMO specifically, the main treatments are anti-VEGF[4] therapy, steroid implants and laser photocoagulation. In recognition of the profound impact of sight preservation on patients' quality of life, NHS England is committed to providing patients with high-quality, cost-effective care for DMO, whilst ensuring all those who might benefit from treatment receive it.

Ophthalmology is the NHS's highest-volume outpatient specialty, with over 7.5 million appointments annually. Anti-VEGF therapy remains the cornerstone of treatment, yet significant variation exists across the country in how first-line regimens are delivered and monitored. With an ageing population driving demand and extensive waiting lists straining capacity, the system is under increasing pressure. Inconsistent treatment monitoring across NHS Trusts further complicates the collection of real-world data, making it difficult to evaluate outcomes and treatment durations effectively.

In response to these challenges, NHS England launched a comprehensive programme in 2024 to evaluate current and future treatment pathways within medical retinal services, with a focus on wet age-related macular degeneration, diabetic macular oedema, and retinal vein occlusion. The programme highlighted the need for a unified national treatment pathway, providing clear guidance on starting, switching, and stopping criteria to ensure patients

[1] Macular Society (2025). Diabetic macular oedema. Accessed 09/10/2025.
[2] Diabetes UK (2025). How many people in the UK have diabetes. Accessed 09/10/2025.
[3] Minassian et al (2012). Prevalence of diabetic macular oedema and related health and social care resource use in England. *Br J Ophthal*.96:345-349.
[4] anti-VEGF: anti–vascular endothelial growth factor treatments injected into the eye.

receive optimal treatment at the appropriate stage. Additionally, a review of treatment data was conducted to identify the most cost-effective options while addressing ongoing capacity limitations.

The updated Commissioning framework for best value biological medicines sets out NHS England's ambitions to establish a best value first approach, by accelerating and widening the adoption of best value biological medicines across the NHS – emphasising the importance of a collaborative approach.

In recognition of the profound impact of sight preservation on patients' quality of life, NHS England is committed to providing patients with high-quality, cost-effective care for RVO, whilst ensuring all those who might benefit from treatment receive it.

The treatment pathway aims to support NHS commissioners and their system partners in England with commissioning of NICE approved treatments at the right point in the patient pathway. This will ensure patients have access to the best value treatments at the right point.

The goal of developing national pathways is to reduce the considerable variation across England and to optimise use of the treatments available. These documents will support the 'should cost, 'should deliver' approach to commissioning as highlighted in the model ICB blueprint.

This pathway was developed, in conjunction with input from a national expert working group, led by Louisa Whickham, National Clinical Director for Eye Care and Luke Nicholson, Director Medical Retinal Services, Moorfields NHS Trust.

The group consisted of clinicians, commissioners, pharmacists, patients and service managers across England. Recommendations made in this pathway were based on NICE guidance and clinical consensus supported by published clinical trial data.

3. Key recommendations

- Our analysis, combining both clinical trial data and real-world evidence, shows that adopting a treat-and-extend approach as standard—**with aflibercept 2mg biosimilar**—achieves the same patient outcomes at a lower cost. This makes it the best value option and should be used first line alongside **ranibizumab biosimilar**.

- 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**.

- This treatment pathway offers a best value approach as a whole and outlines criteria that enable switching if patients don't respond fully to treatment or if they don't reach the expected dosing interval within a specific time interval. Adopting biosimilars helps unlock system-wide benefits and frees up resources to be reinvested into patient care.

- We will be working with the NHS England GIRFT team to support best practice recommendations in ophthalmology services and address any remaining concerns around capacity.

4. Implementation through NHS commissioning and contracting systems

This guidance sets out how best value can be locked in from the start when initiating new patients and ensures that the largest number of patients can benefit from therapeutic advances.

Collaborative working across the system – commissioners, providers and their clinical teams – is essential for the quick and consistent realisation of the potential savings and any other benefits from a switch to a best value biological medicine.

Following focused system engagement, we have identified key enablers in both planning for the availability of a biosimilar and implementation into clinical practice; overarching these is

robust and timely communication between the national and regional leadership teams, professional networks and provider trusts.

i. Good clinical leadership and accountable person(s) including clinical champions locally.
ii. Implementation support for clinicians and dedicated multi-disciplinary switch teams at provider level.
iii. Utilising the specialist pharmacy service preparedness checklist once available.
iv. Standardised consent (and where necessary re-consent) process (see pathway).
v. Patient communication materials to help support shared decision making as appropriate.

Assessment of the Opportunity

Commissioners should assess the opportunity available to them from implementing the proposed pathway and work with their local trust and clinical teams to identify key savings opportunities using the DMO calculator, whilst identifying any variation to the proposed approach with their local Trusts.

These documents are working documents and aim to support systems with planning for implementation of biosimilar aflibercept once available. Systems should use the existing cost calculator for DMO to identify any savings associated with:

a) Patients currently already prescribed aflibercept originator product and the potential savings associated with switching existing patients to a biosimilar once available.
b) Identification of potential patients that could be switched away from 2nd or options if clinically appropriate and not previously tried.
c) Savings associated with new patients starting on aflibercept biosimilar once available.

The pathway clearly identifies when a recommendation has been made on usual or best practice or clinical consensus.

Resource Implications

We have considered the drug and activity costs in our pathway. The drug acquisition costs of aflibercept 2mg biosimilars and ranibizumab biosimilars are the lowest compared to the newer agents. The cost calculator, provided separately, serves as a guide for commissioners to estimate costs involved for the drug options chosen whilst balancing capacity constraints.

The tool references list prices and 2025/26 NHSPS Annex A workbook prices, which can be amended with local pricing arrangements to reflect true local costs.

Treatment modelling summary

Based on NHS England modelling, **first-line treatment with either ranibizumab biosimilar or aflibercept 2mg biosimilar offers the best-value**. Therefore, **it is recommended to start patients with ranibizumab biosimilar or aflibercept 2mg biosimilar first before moving on to other treatments.**

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**.

Monotherapy options:

- Faricimab and aflibercept 8mg require marginally fewer appointments (12) compared to ranibizumab (15) and aflibercept 2mg (14) over 3 years.
- Despite the higher appointment frequency, aflibercept 2mg biosimilar and ranibizumab biosimilar remain as the best value options.

Single switch options:

Regardless of which anti-VEGF was used first:

- Aflibercept 2mg ↔aflibercept 8mg sequence has the least amount appointments over 3 years (14 -15). Faricimab ↔ aflibercept 8mg sequence results in slightly fewer appointments over 3 years (16) compared to:
    - Ranibizumab biosimilar➔faricimab sequence (17 appointments)
    - Ranibizumab biosimilar➔aflibercept 8mg sequence (18 appointments)
    - Aflibercept 2mg biosimilar➔faricimab sequence (17 appointments)
    - Aflibercept 2mg biosimilar ↔ ranibizumab biosimilar combination (18 appointments)
- Although the aflibercept 2mg biosimilar ↔ ranibizumab biosimilar combination has the highest number of appointments over 3 years, it remains the best value option.
- The faricimab-aflibercept 8mg combination is the most expensive.

Double switch options:

- **Combinations containing ranibizumab biosimilar-aflibercept 2mg biosimilar offer the better value despite having 22-23 appointments over 3 years.**
- Combinations containing faricimab-aflibercept 8mg have marginally lesser number of appointments (19-21 appointments over 3 years). Costs across the other double switch combinations are similar, with no significant differences.

Purpose of tables 1 to 4

Tables 1 to 4 are designed to compare the number of appointments per patient over 3 years and the cost per appointment for different treatment sequences involving:

- Monotherapy
- Single switch
- Double switch

Each table corresponds to a different first-line drug:

- Ranibizumab biosimilar
- Aflibercept 2mg biosimilar
- Faricimab
- Aflibercept 8mg

How to read the tables

Each table is structured as a matrix:

- Rows represent the second-line drug.
- Columns represent the third-line drug.
- Cells show the total number of appointments over 3 years for that treatment sequence.
- NE = Not Evaluated (i.e., that combination was not modelled).

Steps to use the tables

1. Identify the first-line drug you are interested in (e.g., ranibizumab biosimilar).
2. Locate the corresponding table for that first-line drug.
3. Compare appointment numbers across different second- and third-line combinations.
4. Use the legend to interpret cost tiers per appointment for each combination.
5. If the same drug name appears in all three columns, this represents monotherapy. If the same drug name appears in two columns, this represents single switch.

Modelling assumptions to keep in mind

Refer to DMO cost calculator for full details

- Injection frequency was populated based on a combination of clinical trial and real-world data, supplemented by assumptions based on clinical consensus from the expert working group.
- For **aflibercept 8mg**, a conservative modelling (**dose extension up to 20 weeks**) was applied instead of the SPC recommendations (24 weeks) due to lack of real-world experience.
- **Monotherapy:** treat-and-extend protocol after initial loading.
- **Single switch:** switch at month 5
- **Double switch**: switch at months 5 and 12.

Legend: Average cost per appointment over 3 years (drug + activity cost)

	Best value
	Mid-tier
	Highest tier
NE	Not evaluated

How cost was calculated

Average cost per appointment over 3 years = Total cost (drug + activity) over 3 years / Number of appointments over 3 years

Table 1. Number of appointments per patient over 3 years, with ranibizumab biosimilar as first line drug

First line drug	Second line drug	Third line drug			
		Ranibizumab	Aflibercept 2mg	Faricimab	Aflibercept 8mg
Ranibizumab biosimilar	Ranibizumab	15	NE	NE	NE
	Aflibercept 2mg	NE	18	23	23
	Faricimab	NE	22	17	21
	Aflibercept 8mg	NE	22	21	17

Table 2. Number of appointments per patient over 3 years, with aflibercept 2mg biosimilar as first line drug

First line drug	Second line drug	Third line drug			
		Ranibizumab	Aflibercept 2mg	Faricimab	Aflibercept 8mg
Aflibercept 2mg biosimilar	Ranibizumab	NE	NE	NE	NE
	Aflibercept 2mg	NE	14	NE	NE
	Faricimab	NE	NE	17	19
	Aflibercept 8mg	NE	NE	21	15

Table 3. Number of appointments per patient over 3 years, with faricimab as first line drug

First line drug	Second line drug	Third line drug			
		Ranibizumab	Aflibercept 2mg	Faricimab	Aflibercept 8mg
Faricimab	Ranibizumab	NE	NE	NE	NE
	Aflibercept 2mg	NE	17	NE	21
	Faricimab	NE	NE	12	NE
	Aflibercept 8mg	NE	20	NE	16

Table 4. Number of appointments per patient over 3 years, with aflibercept 8mg as first line drug

First line drug	Second line drug	Third line drug			
		Ranibizumab	Aflibercept 2mg	Faricimab	Aflibercept 8mg
Aflibercept 8mg	Ranibizumab	NE	NE	NE	NE
	Aflibercept 2mg	NE	14	21	NE
	Faricimab	NE	20	16	NE
	Aflibercept 8mg	NE	NE	NE	12

5. 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 a line of therapy: • Switch from branded to biosimilar and vice versa, biosimilar to biosimilar switches for the same agent • Switch back to a previous anti-VEGF (i.e. those who did not experience clinical benefit after failed extended interval attempts with newer agents) • Switch due to adverse drug events or allergy Worked examples One line of therapy: • Patient switched from branded drug A to biosimilar drug A • Patient switched from drug A to B due to adverse drug events Two lines of therapy: • Patient had suboptimal response to drug A, now on drug B • Patient had suboptimal response to drug A, switched to drug B and had a good clinical response. Unable to extend dose intervals beyond 7 weeks so switched to drug C. Still unable to extend dose intervals on drug C and no clinical benefit, so switchback to drug B because it is more cost-effective. Three lines of therapy: • Patient who had suboptimal responses to drugs A and B, now on drug C • Patient had suboptimal response to drug A, then switched to drug B. Unable to extend dose intervals beyond 7 weeks on drug B so switched to drug C. Remains on drug C because has added clinical benefit compared to drug B even though unable to extend dose intervals further.
Recommendations for best practice	Recommendations made by the expert working group following review of real-world evidence or based on consensus from expert working group. These are subject to local commissioning agreements.
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.

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.

See local adaptations on cover sheet

6. 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 → **NG242 criteria (not mandated)**
CRT < 400 microns

YES

Treatment options (see Note 5)

	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)	

Treatment options (see Note 4)

- **Macular laser**
- **Anti-VEGFs** Aflibercept 2mg biosimilar OR Ranibizumab biosimilar

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.

NICE TA CRT ≥ 400 microns

NO – switch to alternative preparation

SWITCH treatment if (see Note 7):
- 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)

NG242 CRT <400 microns

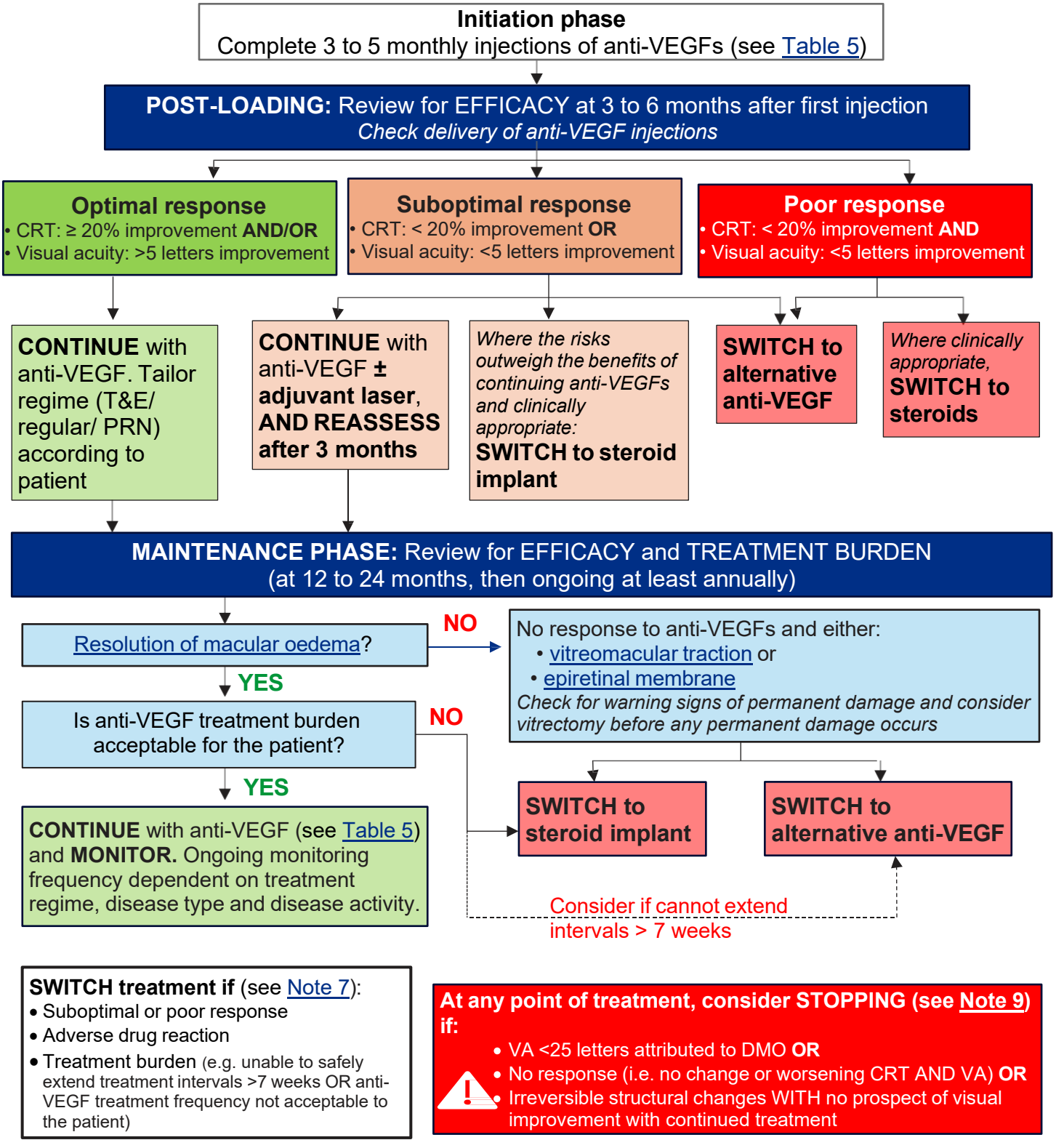
Second-choice anti-VEGFs may be considered first-line for the following reasons (see Note 5):
- Capacity constraints
  - Note this may not be cost-effective in the long-term and needs to be agreed locally with commissioners
- Patient factors
- Clinical factors

At any point of treatment, consider STOPPING (see Note 9) 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

See local adaptations on cover sheet

Figure 1. Recommended anti-VEGF efficacy and treatment burden check time points (see Note 6, Note 7 and Note 8)



SWITCH treatment if (see Note 7):
- 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 9) 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 7)

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.

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.

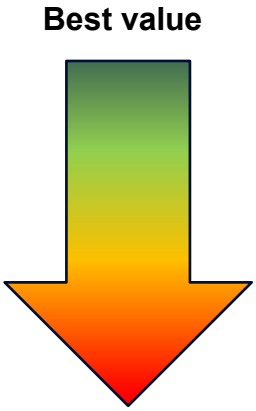
For patients with baseline ETDRS < 69 letters, Protocol T study demonstrated efficacy hierarchy for the following drugs: aflibercept (most efficacious) > ranibizumab > bevacizumab (least efficacious).[1210] There is lack of evidence which directly compares the efficacy hierarchy for all anti-VEGFs which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

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. In clinical practice, therapeutic effect can last for 4 months and may require earlier retreatment (off-label).[13] The expert working group is unable to clinically define this cohort.	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. Clinicians report no concerns and the number of patients requiring this is small. Subject to local commissioning, it is recommended to commission up to 3 implants per year (or treatment every 4 months) [off-label] until the patient meets discontinuation criteria (see Note 5 and Note 9).
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, rescue treatments (e.g. anti-VEGFs, laser, dexamethasone implant) are recommended whilst on fluocinolone implant (see Note 5). This affects approximately 40% according to the FAME study and IRISS registry study.[14,15] 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)
Dexamethasone implant (4 monthly/ 3 implants per year)
Fluocinolone implant (2 implants over 3 years)

NB: The cost of rescue treatments needed for fluocinolone implant is not included in the model.

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.

7. 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/

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: Use of anti-VEGFs in patients with visual impairment with CRT < 400 microns below NICE TA treatment threshold

NICE NG242 (not mandatory) recognise the use of anti-VEGFs below the NICE TAs CRT treatment threshold.[1]

Recommendations for best practice:

Recommendation 2. Consider offering anti-VEGFs (subject to local agreement) or macular laser treatment for patients with CRT < 400 microns. Use aflibercept 2mg biosimilars or ranibizumab biosimilars as treatment options for this cohort of patients.

Rationale:

Savings incurred from the “biosimilars first” approach could be used to fund non-NICE TA recommendations. The expert working group recommends the use of biosimilars for this purpose because it would be more affordable for the NHS compared to other newer anti-VEGFs. We are unable to estimate the size of this cohort.

Extract from NICE NG242, evidence review G, section 1.1.12.4: [1]

Anti-VEGFs are only considered to be cost-effective for people with central retinal thickness of 400 micrometres or more in the technology appraisals. The committee discussed how some people, such as women and people of South Asian or Afro-Caribbean descent tend to have thinner retinas. This means that even if they have retinal thickening, they may not reach, or will take longer to reach, the 400 micrometre threshold, and may therefore miss out on important treatment, which could lead to greater loss of vision. Given that the network meta-analyses in the NICE review showed anti-VEGFs to be clinically and cost-effective for a wider population, and the meta-analysis indicated that there may be some benefits to the use of anti-VEGFs in this group, the committee decided to recommend that anti-VEGFs are considered for people with central retinal thickness of less than 400 micrometres. With more limited evidence for people with thinner retinas, and an awareness that macular laser can have benefits, they did not think they could make as strong a recommendation in favour of anti-VEGFs as for those in the subgroup with greater central retinal thickness. Macular laser was recommended as the alternative option for this group. Although the analysis suggests that some anti-VEGFs may be most effective, macular laser can also be effective and is current practice for many people in this group because of the 400 micrometre threshold in the NICE technology appraisal guidance. It also has the benefit of delaying the need for anti-VEGF treatment for some people.

Note 5: 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.

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 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
    - 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 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.

Recommendation 8. For dexamethasone implant, it is recommended to commission up to 3 implants per year (treatment every 4 months) [off-label] until the patient meets discontinuation criteria [off-label] (see Note 9). Consider switching to fluocinolone implant if 4-monthly dexamethasone is required.

Rationale:

NICE TA824 conducted the economic modelling for dexamethasone implant based on 6-monthly dose intervals for up to 3 years (six implants in total). In clinical practice, therapeutic effect can last for 4 months and may require earlier retreatment (off-label).[13] Frequent and

repeated treatments would increase the risk of adverse events and needs to be discussed with the patient.

Subject to local agreement, it is recommended to commission up to 3 dexamethasone injections per year (treatment every 4 months). It is expected that the proportion of patients who will require 3 injections per year is small. The expert working group is unable to clinically define this cohort. Consideration should be given to switch this cohort to fluocinolone implant if appropriate.

The manufacturer reports no experience of the efficacy or safety on repeat administration in DMO beyond seven implants and it would be an off-label use.[20] However, it is recognised that some patients may benefit from repeated administration beyond seven implants. Clinical experience supports this, with no safety or efficacy concerns associated with administration beyond seven implants. It is expected that the number of patients who will require seven or more implants is small. We recommend patients who received benefit on dexamethasone to continue with treatment beyond seven implants until discontinuation criteria apply (off-label use, see also Note 9).

Recommendation 9. Subject to local commissioning, rescue treatments (e.g. anti-VEGFs, laser, dexamethasone implant) are recommended for patients on fluocinolone implant.

Rationale:

Approximately 40% of patients on fluocinolone may need rescue treatments (e.g. anti-VEGFs, laser, dexamethasone implant) (FAME study and IRISS registry study).[14,15] Commissioning of rescue treatments would be subject to local commissioning. We are unable to estimate the costs of rescue treatments because it would vary between patients.

Note 6: Monitoring recommendations

Recommendation 10. 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.

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 11. 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 12. For anti-VEGFs, consider treatment burden and efficacy assessment at 12 to 24 months from the start of treatment. See Note 7 if treatment switch to steroid implants or alternative anti-VEGF is indicated.

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 13. 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 14. 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 7: Treatment switch considerations

Recommendation 15. 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 16. If patients are switched from an anti-VEGF to a steroid implant, monitor patients for neovascularisation.

Rationale:

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

Recommendation 17. 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 18. 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]

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 19. 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 20. 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 21. 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)

  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 22. 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 5, recommendation 8)

Note 8: 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]

Note 9: 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 8)

  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 24. Treatment STOP recommended if, despite optimum treatment:

- visual acuity < 15 letters attributable to DMO in the absence of other pathology (see also Note 8)

  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

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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9. Acknowledgements

Luke Nicholson, Director Medical Retinal Services, Moorfields NHS Trust and all members of the National Medical Retinal Expert Working Group and Commissioner Forum.

South West London ICB, South West London Diabetic Macular Oedema Drug Pathway, Sep 2022.

Revision history

Revision date	Summary of changes	Version
17/10/2025	Commissioning guidance published	V1.0