Hertfordshire and West Essex Integrated Care System

NHS Hertfordshire and West Essex Integrated Care Board

Commissioning Guidance: Medical Retinal Treatment Pathway in Macular Oedema Secondary to Retinal Vein Occlusion

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Table of Contents

1. Abbreviations 3

2. Key recommendations 4

3. Definitions 5

4. Treatment algorithm for macular oedema secondary to RVO 6

5. Notes 10

6. References 21

7. Acknowledgements 22

1. Abbreviations

Abbreviation	Explanation
BCVA	Best corrected visual acuity
BRVO	Branch retinal vein occlusion
CI-MO	Centre-involving macular oedema
CRVO	Central retinal vein occlusion
CMT	Central macular thickness
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.
OCT	Optical coherence tomography
PRN	*Pro Re Nata* (more commonly known as when necessary)
RCOphth	The Royal College of Ophthalmologists
RVO	Retinal vein occlusion
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
VA	Visual acuity
VEGF	Vascular endothelial growth factor

2. 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.** Aflibercept 8mg is not approved for use in RVO.

- 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.

- There are no head-to-head studies which directly compares the injection frequencies for ranibizumab, aflibercept 2mg and faricimab. The LEAVO study is the only randomised controlled trial which compared the use of aflibercept 2mg against ranibizumab (PRN regimen in CRVO patients). The cost tiers for these drugs were calculated based on the assumptions extrapolated from LEAVO and COMINO/ BALATON trials.[12-14]

Table 1. Anti-VEGF dose frequency extrapolated from trial data

Drug	Aflibercept 2mg	Ranibizumab	Faricimab
Number of injections over 2 years, based on PRN regimen	10.0	11.8	10.0*

**No head-to-head data. COMINO/ BALATON trial demonstrated that faricimab is non-inferior to aflibercept 2mg at 24 weeks but no injection frequency comparison between aflibercept 2mg and faricimab. It is assumed that faricimab would require the same number of injections as aflibercept 2mg for the purpose of cost modelling.*

- 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.

3. Definitions

Term	Explanation
Favourable disease outcome	Resolution of centre-involving oedema
Unfavourable disease outcome	Reduction in disease activity on OCT but with signs of active disease. E.g. reduced but persistent centre-involving oedema
Poor disease outcome	• VA: No change or worsening • OCT: No change or worsening CMT
Fellow eye	The eye opposite the one being treated
Line of therapy	The order in which different therapies are given to people as their disease progresses. A switch from originator to biosimilar does not count as an additional line of therapy.
Recommendations for best practice	Recommendations made by the expert working group following review of real-world evidence or based on consensus from expert working group. These are subject to local commissioning agreements.
Stopping treatment/ permanent discontinuation	A point in the patient's treatment journey where clinicians decide to stop treatment permanently. This is usually when further treatment is unlikely to benefit the patient.
Treatment harmonisation	The act of using only one drug for both eyes. Usually occurs when one eye is already on treatment, but the other eye qualifies for another treatment.
Treat and extend protocol	A standard treatment regimen for treating RVO, where the interval for the next anti-VEGF injection is extended by 2 to 4 weeks up to a maximum of 16 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 acuity of < 15 letters	This is equivalent to Snellen meter score < 6/150, or logMAR < 1.4
Visual acuity of < 25 letters	This is equivalent to Snellen meter score < 6/96, or logMAR < 1.2
Worse-seeing eye	Also known as the weaker eye. This occurs when one eye sees significantly better than the other eye.

4. Treatment algorithm for macular oedema secondary to retinal vein occlusion (RVO)

Choice of treatment between anti-VEGFs or steroid implants will need to consider risk of IOP, cardiovascular risk, cataract formation and injection frequency.
If more than one treatment is suitable, use the best value treatment based on the overall costs (drug and service delivery).
Prescribe by brand and use best value brand available locally.

Branch retinal vein occlusion (BRVO)

First line treatment options (see Note 3)

Anti-VEGFs
Aflibercept 2mg- switch to biosimilars once available (TA409) OR Ranibizumab biosimilars§ (TA283)

OR
Grid laser photocoagulation

OR
Steroid implant
Dexamethasone (TA229)§

§ NICE TAs mandate these treatments can only be used if laser has not been beneficial, or not suitable due to extent of macular haemorrhage. In clinical practice anti-VEGFs are favoured ahead of laser treatment for most patients.

Central retinal vein occlusion (CRVO)

First line treatment options (see Note 3)

Anti-VEGFs
Aflibercept 2mg- switch to biosimilars once available (TA305) OR Ranibizumab biosimilars (TA283)

OR
Steroid implant
Dexamethasone (TA229)

Is there evidence of response to treatment? (see also Note 7)
Assess response based on visual acuity and disease activity? Check delivery of anti-VEGF injections.

For **anti-VEGF**s: See Figure 1 for schematic illustration. First review before 4th injection.
For **steroids:** Monitoring intervals determined by clinician (see Note 5).

YES

Anti-VEGFs: Continue with either **T&E** (see Table 2) or **PRN** regimen. T&E preferred (see Note 6)
Steroids: Continue treatment (see Table 3)

Monitoring intervals determined by clinician (normally not less than 4-weekly for **anti-VEGFs**) (see Note 4)

The management of the patient should be reviewed by a senior clinician **post-initiation** 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):
- Unfavourable or poor disease outcome
- Adverse drug reaction
- Treatment burden (e.g. anti-VEGF treatment frequency not acceptable to patient)

Subsequent line treatment options

Anti-VEGFs
Aflibercept 2mg- switch to biosimilars once available (TA409) OR Ranibizumab biosimilars§ (TA283) OR Faricimab (TA1004)

OR
Steroid implant
Dexamethasone (TA229)

Subsequent line treatment options

Anti-VEGFs
Aflibercept 2mg- switch to biosimilars once available (TA305) OR Ranibizumab biosimilars (TA283) OR Faricimab (TA1004)

OR
Steroid implant
Dexamethasone (TA229)

Anti-VEGFs- additional information (see Note 6)
If the patient failed at least **TWO** extended interval attempts for subsequent **anti-VEGF** and there is no clinical benefit, **SWITCH BACK** to previous anti-VEGF if it was previously effective, more cost-effective and clinically appropriate.
Consider switching to an **alternative anti-VEGF** or **steroid implant** if this is the patient's second anti-VEGF.

Sequential treatment: A limit on the number of different anti-VEGFs which should be commissioned in RVO is currently not stipulated.

At any point of treatment, consider STOPPING PERMANENTLY if (see also Note 7, Note 8)**:**
- BCVA <25 letters attributed to RVO **OR**
- No response (i.e. no change or worsening CI-MO compared to baseline) **OR**
- Complete resolution of CI-MO with no potential for visual acuity improvement

Steroid implants- additional information
Examples where steroid is more appropriate (see Note 3)**:** recent (within 6 months) cardiovascular events, unable to comply to anti-VEGFs injection frequency (patient factors), pregnancy (if benefits outweigh risks).

SWITCH BACK to anti-VEGF from steroid implants (see Note 6) if patient had a better response (disease activity/ treatment intervals/ functional outcome) whilst on anti-VEGF compared to steroid implants OR adverse drug reaction.

Subject to local commissioning, a maximum of **THREE** steroid implants per year (or treatment every 4 months) [off label] is recommended until the patient meets discontinuation criteria [off-label] (see Note 3 and Note 8).

Figure 1. Schematic illustration of anti-VEGF monitoring for RVO

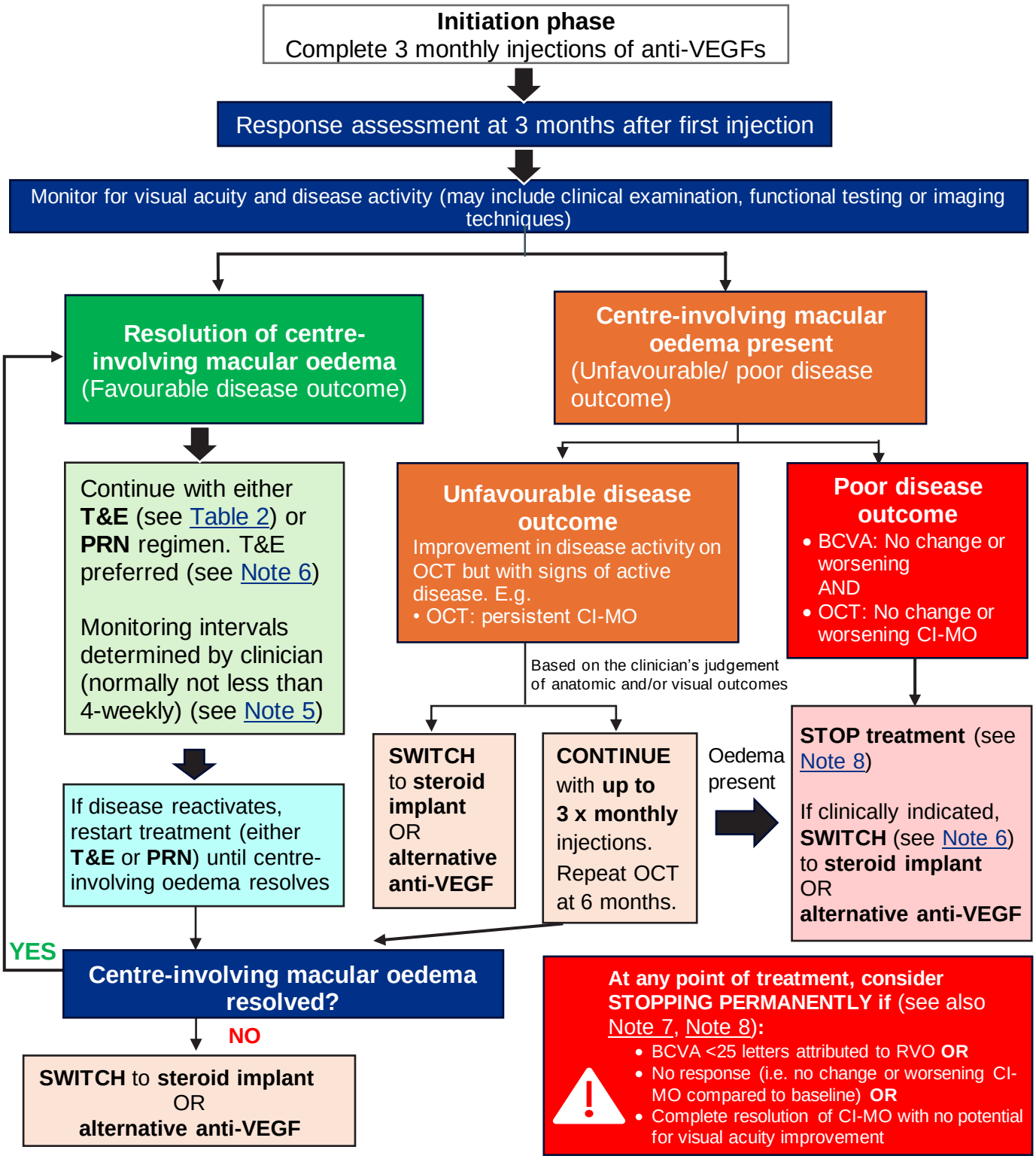

Table 2. Anti-VEGF dosing details according to SPC recommendations

Anti-VEGF	Cost tier	Initiation phase	Maintenance phase	Treat-and-extend (T&E) dose increment intervals	Minimum T&E dose intervals
General information for all anti-VEGFs: Consider switch to steroid implant if recent (within 6 months) cardiovascular events, unable to comply to injection frequency with antiVEGFs (see also Note 6) Aflibercept 8mg is not licensed for use in RVO.					
First line					
Aflibercept 2mg (TA305, TA409) Biosimilars once available	**£££** **£**	1 injection per month until maximum visual acuity is achieved and/or there are no signs of disease activity. Three or more consecutive, monthly injections may be needed. **In practice this is normally 3 to 6 injections.**	If there is no change in disease activity, maintenance therapy could be according to a treat-and-extend regimen or a PRN treatment regimen Treat-and-extend regimen: 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 (CMT worsens compared to baseline), the treatment interval should be shortened accordingly. In CRVO, RCOphth guidance recommends the following: "*once this interval to recurrence is identified, it is advisable to maintain on this interval for a 6-month period before extending again*"	Not specified in SPC, insufficient data to conclude maximum treatment intervals	4 weeks
Ranibizumab 0.5mg biosimilars (TA283)	**£**			Not specified in SPC, insufficient data to conclude maximum treatment intervals	4 weeks
Second line					
Faricimab 6mg (TA1004)	**££**			Up to 4 weeks. Max treatment interval 16 weeks (no data for > 16 weeks intervals)	4 weeks*

Cost tier per annum (drug and activity) based on number of doses expected per annum **£** (cheapest) to **£££** (most expensive) from NHSE modelling (see Table 1) at the time of writing.

*Faricimab off-license dosing: 3 weekly was used in studies to allow flexibility of dose scheduling.[16,17]
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 faricimab.

Table 3. Steroid implant dosing details according to SPC recommendations

Intravitreal steroid implant	Dose	Other notes
Dexamethasone intravitreal implant (TA824) **2 injections per year ££** **3 injections per year £££**	700 micrograms (one implant) intravitreally into the affected eye. Repeat doses should be considered when a patient experiences a response to treatment followed subsequently by a loss in visual acuity and in the physician's opinion may benefit from retreatment without being exposed to significant risk. **Patients who experience and retain improved vision should not be retreated** Patients who experience deterioration in vision, which is not slowed by dexamethasone should not be retreated (consider stopping permanently, see (see Note 8).	Administration to both eyes concurrently is not recommended. RCOphth guidance states that if this is used as first line, re-treatment at every 4 (off-label) to 6 monthly (licensed) intervals may be required until visual stability is obtained. The occasional patient may require treatment at 3 months (off-label). However, repeated and frequent treatments will increase the risk of adverse events and these should be discussed with the patient. [1] NICE TA only included 6-monthly intervals in their economic assessment. 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 [off-label] (see Note 3 and Note 8).

Table 4. Estimated Loss of Exclusivity (LoE)[15]

Drug	LoE
Ranibizumab	July 2022
Aflibercept 2mg	End of November 2025 (8mg not licensed in RVO)
Faricimab	2037
Dexamethasone implant	2026 (no planned generics launch in UK)

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.

5. Notes

Note 1: Treatment goals (for both BRVO and CRVO)

- Resolution of macular oedema (RCOphth guidance)[1]
- Improvement in visual acuity (RCOphth guidance)[1]
- Manageable treatment burden for the patient

However, it is recognised that not all patients can achieve improved visual acuity 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 of all treatment possibilities at the outset. This would include:

- Expected treatment options, outcomes and treatment burden with patients.
- Potential treatment changes throughout their journey, including the use of best value medicines when they become 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/retinal-vein-occlusion/

Note 2: Service delivery by other healthcare professionals

Some SPCs (e.g. Ongavia®) mandate administration by "a qualified ophthalmologist experienced in intravitreal injections". However, in practice this may be administered by a suitably trained healthcare professional (HCP). RCOphth guidance acknowledges this and recommends that '*it is essential that the HCP always has immediate access to advice from an ophthalmologist whilst giving injections and an appropriately trained clinician is available on site to deal with any very urgent complications'*.[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 3: 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 treatment (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.[10] Use best value brand available locally.

Recommendations for best practice:

Recommendation 2. For BRVO, ranibizumab can be used first line without the need to trial grid laser photocoagulation.

Rationale:

- While NICE TAs recommend grid laser photocoagulation as first line for both ranibizumab (NICE TA 283) and dexamethasone (NICE TA 229), it is often not the first-line treatment in current practice.

- Grid laser is often not practical due to its inferior efficacy and the need for well-controlled blood pressure.[10,11] It is generally used as an additional option for patients who cannot tolerate injections. NHS England is working with NICE to update its guidance.

Recommendation 3. For **BRVO,** the following **anti-VEGF sequence** is recommended where clinically appropriate:

First line: Aflibercept 2mg- switch to biosimilar once available (TA409) OR ranibizumab biosimilar (TA283)

Second line onwards: First line options OR faricimab (TA1004)

Rationale:

- There is limited real-world data directly comparing all anti-VEGF treatments for BRVO. As a result, current recommendations are primarily based on clinical trial evidence.

- The BALATON clinical trial demonstrated that faricimab is non-inferior to aflibercept 2mg at 24 weeks.[12] The sequence in which treatments are administered does not affect the efficacy of faricimab. A follow-up study from this trial found only marginal differences in efficacy, treatment intervals, and safety—regardless of whether faricimab or aflibercept 2mg was used first.[13] There is no clinical trial which compared the treatment intervals between anti-VEGFs.

- Given the minimal differences in outcomes and the lack of robust real-world comparative data, NHS England recommends starting treatment with better value agents—such as aflibercept 2mg or ranibizumab biosimilars—before considering more expensive options like faricimab. 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. For **CRVO,** the following **anti-VEGF sequence** is recommended where clinically appropriate:

First line: Aflibercept 2mg- switch to biosimilar once available (TA305) OR ranibizumab biosimilar (TA283)

Second line onwards: First line options OR faricimab (TA1004)

Rationale:

- There is limited real-world data directly comparing all anti-VEGF treatments for CRVO. As a result, current recommendations are primarily based on clinical trial evidence.

- **Aflibercept 2mg vs ranibizumab:** The LEAVO study showed that aflibercept 2mg is non-inferior to ranibizumab.[14] This means that the average improvement in vision following treatment for macular oedema due to CRVO was similar between the two drugs. However, **fewer injections are required for aflibercept 2mg**.

- **Faricimab vs aflibercept 2mg:** The COMINO clinical trial demonstrated that faricimab is non-inferior to aflibercept 2mg at 24 weeks.[12] The sequence in which treatments are administered does not affect the efficacy of faricimab. A follow-up study from these trials found only marginal differences in efficacy, treatment intervals, and safety—regardless of whether faricimab or aflibercept 2mg was used first.[13] There is no clinical trial which compared the treatment intervals between the anti-VEGFs.

- Given the minimal differences in outcomes and the lack of robust real-world comparative data, NHS England recommends starting treatment with better value agents—such as aflibercept 2mg or ranibizumab biosimilars—before considering more expensive options like faricimab. 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 5. Consider the use of **steroid implants over anti-VEGFs** if:

- Recent cardiovascular events within the last 6 months
- Unable to comply with anti-VEGF injection frequency (patient factors)
- Pregnancy, provided the benefits of treatment outweigh the risk

Rationale:

- Limited safety data in patients with prior history of stroke or transient ischaemic attacks or myocardial infarction within the last 6 months.[8]
- Anti-VEGFs are not recommended for use in pregnancy because it is potentially teratogenic and embryo-/ foetotoxic.[8]

- **Patient factors:** some patients cannot comply with anti-VEGF injection frequency and may be better managed with steroid implants, which would require a smaller number of injections compared to anti-VEGFs. Examples of patient groups include:
    - learning difficulties
    - dementia
    - hospital transport
    - requiring treatment in the operating theatre under sedation/deep sedation/general anaesthesia
    - frequent inpatient hospital admissions or other regular attendance (e.g. chemotherapy)
- Patients on steroid implants may require re-treatment at 4 months (off-label) to 6 monthly intervals until visual stability is obtained. The occasional patient may require treatment at 3 months (off-label).[1]
- Frequent and repeated treatments with steroid implants would increase the risk of adverse events and needs to be discussed with the patient.

Recommendation 6. Where one eye is already on **anti-VEGF** treatment, but the other eye qualifies for another **anti-VEGF** treatment, prioritise treatment harmonisation by choosing the best treatment options 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. For dexamethasone implant (subject to local commissioning), 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 8).

Rationale:

NICE TA 229 conducted the economic modelling for dexamethasone implant based on 6-monthly dose intervals for up to 3 years.[7] In clinical practice, therapeutic effect can last for 4 months and may require earlier retreatment (off-label). The occasional patient may require treatment at 3 months (off-label).[1] NICE TA 229 (section 4.11) states that “although the

safety data relate to 6-monthly treatment, it is expected that clinicians may re-treat at 4 months in clinical practice, but may not treat more frequently because of the risk of adverse events from the accumulation of dexamethasone in the eye." [7]

It is recommended to commission up to 3 dexamethasone implants per year (treatment every 4 months) [off label], subject to local agreement. It is expected that the proportion of patients who will require 3 implants per year is small. The expert working group is unable to clinically define this cohort or estimate the proportion of patients who will require 3 implants per year.

There is limited clinical trial data on the efficacy and safety of repeat administration in RVO beyond two implants. NICE TA 229 (section 3.17) estimated up to six implants may be needed in practice. However, it is recognised that some patients may benefit from repeated administration beyond six implants. Clinical experience supports this, with no safety or efficacy concerns associated with administration beyond six implants. It is recommended that patients who received benefit on dexamethasone to continue with treatment beyond six implants [off-label], until discontinuation criteria apply (see Note 8 for discontinuation criteria).[18]

Note 4: Monitoring recommendations at follow-up visits

Recommendation 8. For both **BRVO and CRVO:** Monitor visual acuity and disease activity. Disease activity monitoring may include clinical examination, functional testing or imaging techniques (e.g. optical coherence tomography or fluorescein angiography). Monitoring intervals would be determined by the clinician based on individual patient's response and disease type. Please refer to Section 7 of RCOphth guidance.

Recommendation 9. For steroid implants, monitor for raised IOP (which peaks at day 60) at and formation or progression of cataract. Monitoring intervals would be determined by the clinician based on individual patient's response and disease activity.

Rationale:

Recommendations 8 and 9 were based on RCOphth guideline.[1]

Recommendation 10. The management of the patient should be reviewed by a senior clinician post-initiation and annually to consider if continuation of treatment is in patient's best interest.

Note 5: Treatment regime

Recommendation 11. Treat-and-extend preferred. **If PRN** regimen is chosen, it is recommended that these patients are monitored **4-8 weekly intervals** and treated appropriately for optimal visual outcomes.

Rationale:

Fixed monthly injections, PRN and treat-and-extend regimes following a loading phase provide similar visual outcomes (RCOphth guideline).[1] There is a risk of monthly injections in a fixed monthly treatment regimen and requirement for 4-8 weekly appointments in the PRN regimen. Therefore, treat-and-extend is recommended because it offers better use of resources compared to PRN and fixed monthly injections.

Note 6: Treatment switch considerations

Recommendation 12. Switch to **alternative treatment class** if:

- Poor outcome, defined as:
  - Visual acuity: No change or worsening AND
  - Disease activity: No change or worsening centre-involving oedema
- Unfavourable disease outcome, defined as:
  - Reduction in disease activity on retinal imaging but with signs of active disease. E.g. persistent centre-involving oedema
- Adverse events whilst on therapy. Notable adverse events for treatment class include:
  - Anti-VEGFs: cardiovascular events
  - Steroid implants: raised intraocular pressure, cataract formation

Rationale:

There is a good rationale to switch from steroid implants to an anti-VEGF agent and vice versa as the different mode of actions of these agents may aid in resolution of macular oedema (RCOphth guideline).[1]

Recommendation 13. Switch from **anti-VEGFs** to **steroid implant** where clinically appropriate, if:

- Frequent injections required to maintain disease stability and treatment burden is not acceptable to patient (patient factors)
- 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.[8]
- **Patient factors:** some patients cannot comply with anti-VEGF injection frequency and may be better managed with steroid implants, which would require a smaller number of injections compared to anti-VEGFs. Examples of patient groups include:
  - learning difficulties
  - dementia
  - hospital transport
  - requiring treatment in the operating theatre under sedation/deep sedation/general anaesthesia

- frequent inpatient hospital admissions or other regular attendance (e.g. chemotherapy)
- people who may not want to continue with regular anti-VEGF injections for other reasons (e.g. anxiety about injections/ needle phobia)

Recommendation 14. Switch from **anti-VEGF** to **an alternative anti-VEGF**, **only if anti-VEGF is still appropriate** and:

- Patient experiences **poor outcome**, defined as:
  - Visual acuity: No change or worsening AND
  - Disease activity: No change or worsening centre-involving oedema/ CMT
- **Unfavourable disease** outcome, defined as:
  - Reduction in disease activity on OCT but with signs of active disease. E.g. persistent centre-involving oedema

Recommendation 15. A limit on the number of different anti-VEGFs which should be commissioned in RVO is currently not stipulated. The expectation is that the first anti-VEGF used should normally be first choice options.

Rationale:

There is limited evidence for sequential use of anti-VEGFs in RVO, but it is reasonable to trial an alternative anti-VEGF agent where clinically appropriate to avoid the risks of adverse events with steroid implants. 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 16. If the patient failed at least **TWO** extended interval attempts for subsequent **anti-VEGF** and there is no clinical benefit, switch back to previous anti-VEGF if it was previously effective**,** better value and clinically appropriate**.**

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

Rationale:

There is no clinical trial which directly compares all the treatment intervals between anti-VEGFs.

The LEAVO study (ranibizumab vs aflibercept 2mg in CRVO patients) showed that **aflibercept 2mg requires less injections compared to ranibizumab**.[13] There is no evidence that faricimab offers superior injection intervals compared to ranibizumab or aflibercept 2mg. The key trials demonstrated that faricimab is non-inferior to aflibercept 2mg at 24 weeks but there was no specific mention of differences in injection frequency. It is therefore assumed that faricimab would require the same number of injections as aflibercept 2mg with regards it being non-inferior to aflibercept 2mg.

Choosing an alternative anti-VEGF for patients unable to extend injection intervals beyond 7 weeks is a clinical decision, though evidence supporting improved intervals post-switch in RVO is limited.

If appropriate, patients should be allowed TWO extended interval attempts with the new anti-VEGF agent. If both attempts fail and no clinical benefit is observed, switch back to previous anti-VEGF if it was previously effective, better value and clinically appropriate. This recommendation reflects commissioners feedback to support appropriate use of best value medicines throughout the patient's treatment journey.

Recommendation 17. Consider **switchback** from **steroid implant** to **anti-VEGFs** if:

- Initial reason for switch was due to cardiovascular events which has been resolved.
- Patient had a better response (disease activity/ treatment interval/ functional outcome) whilst on anti-VEGF compared to steroid implant.
- Significant rise in intraocular pressure following treatment with dexamethasone implant, normally peaks at 60 days post dexamethasone implant.[9]

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

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

Recommendation 18. REVIEW with consideration to stop treatment if:

- Visual acuity of <25 letters (see also Note 7) attributable to RVO in the absence of other pathology despite optimum treatment OR
- Poor response to treatment (i.e no change or worsening CMT AND visual acuity)

Questions to be considered when deciding whether further treatment is beneficial (discontinue treatment if yes to all the below):

- For anti-VEGFs:
  - Has the patient completed the initiation phase (at least three-monthly injections)?
- Is the patient's intravitreal treatment optimised and adequate (i.e. they have been receiving adequate injections at optimal intervals on time)?
  - *Just over a third of patients will require only 3 anti-VEGF injections to reach maximum VA while another third will require 6 consecutive anti-VEGF injections (RCOphth guideline)*
- Is there another treatment which would be better for the patient?
- Is the treated eye the WORSE seeing eye?
- Does the patient agree that they DO NOT receive continuing benefits from treatment?

Recommendation 19. Treatment STOP recommended if, despite optimum treatment:

- Visual acuity < 15 letters (see also Note 8) attributable to RVO in the absence of other pathology AND is the WORSE seeing eye.

Recommendation 20. Treatment STOP recommended if complete resolution of centre-involving macular oedema with no potential for visual acuity improvement.

Rationale*:*
The above cut off points for visual acuity were based on collective expert opinion from the expert working group.

Where a decision is made to discontinue treatment permanently where risks of giving injections outweigh its potential benefits, normally no further monitoring is required for that eye. Refer to Section 7 of RCOphth guideline for further information.

6. References

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2. The Royal College of Ophthalmologists (2018). Ophthalmic service guidance: intravitreal injection therapy. Revised Aug 2018. Accessed 22/07/24 via https://curriculum.rcophth.ac.uk/wp-content/uploads/2018/02/Intravitreal-Injection-Therapy-August-2018-2.pdf
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Revision history

Revision date	Summary of changes	Version
6th Oct 2025	Commissioning guidance published	V1.0
12th Dec 2025	Cost tiers for Table 2 updated	V1.1