South West London
Diabetic Macular Oedema (DMO) Drug Pathway
Version 2.1

Contents:

Approved by: SWL Integrated Medicines Optimisation Committee
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SWL Drug Pathway - Diabetic Macular Oedema Drug Pathway: High Cost Drug Pathway

Version 2.1 (based on NICE with local adaptations)

Laser photocoagulation if non centre-involving CSMO

Does patient have centre-involving clinically significant macular oedema (CSMO) and impaired vision? (note 1)

No – continue to monitor

Yes

Is central retinal thickness (CRT) ≥ 400 microns?

No – continue to monitor

Yes

Is anti-VEGF treatment suitable?

Yes

Step 1:
1st choice: Ranibizumab biosimilar (TA274) (note 2,4,5) **OR** Aflibercept (TA346) (note 2,4,6)
2nd choice: Faricimab (TA799) (note 2,4,7)
3rd choice: Brolucizumab (TA820) (note 2,4,8)

No

Yes – continue as per SPC (treat-and-extend if possible) (note 5,6,7,8)
If high injection burden with ranibizumab consider switch (note 3)

Has patient benefitted from treatment after 12 months*?

No

Step 2: Dexamethasone intravitreal implant (TA824) (note 9)

Has patient benefitted from treatment after 12 months*?

Yes

Yes – If spikes in IOP with max 2 implants, which does not revert to near baseline with careful therapeutic management, consider switch back to anti-VEGF (note 10)

No – consider switch (back) to anti-VEGF (note 10)

Did patient experience spikes in intra-ocular pressure (IOP) after 2 implants?

Yes – continue

No

Is response considered to be optimal i.e.:
- Sufficient anatomic/functional response **and**
- Patient does not have persistent DMO requiring frequent (4-monthly) dexamethasone implants?

No

Step 3: Fluocinolone intravitreal implant (note 11) (TA953)

Yes – give 2nd implant after 12 months if vision decreases or OCT increases

Has patient benefitted from treatment* **AND** has patient received less than 2 implants?

No

Discontinue high cost drug treatment (note 12)

*Benefit of treatment as evidenced by:
- Stabilised or improved visual acuity **and/or**
- Stabilised or reduced retinal thickness
- Improvement in other anatomical parameters if VA and CRT have deteriorated?

SWL Drug Pathway - Diabetic Macular Oedema Drug Pathway: Notes

Version 2.1 (based on NICE with local adaptations)

Clinicians and commissioners should refer to the relevant technology appraisal and SPC for each drug for further information about eligibility and prescription
Note 1 – CSMO: ETDRS research group defined clinically significant macular oedema (CSMO) DMO, as DMO that threatens the centre of the macula (fovea) [13].
Note 2 – Choosing Treatment: If there is more than one NICE approved treatment available, NICE recommends a discussion between the responsible clinician and the patient about the advantages and disadvantages of each treatment (considering therapeutic need and likely adherence to treatment). If more than one treatment option is suitable, the least expensive will be chosen (taking into account administration costs, dosage and price per dose) unless an order of preference is stated in the TAs. As agreed by the SWL Ophthalmology Medicines Optimisation Clinical Network, and where clinically appropriate, ranibizumab biosimilar should be considered due to cost savings.
Note 3 – Sequential Anti-VEGF Treatment: Patients responding to ranibizumab treatment who require frequent (monthly) treatment, may be switched to an alternate anti-VEGF following a clinical decision[14,15]. If switching to the alternate anti-VEGF has inferior outcomes, a switchback to ranibizumab is allowed[14]. This is a local decision to encourage use of ranibizumab where clinically appropriate. Sequential anti-VEGF treatment in the same eye is not commissioned for non-responders or when aflibercept, faricimab or brolucizumab is selected for treatment naïve eyes.
Note 4 – Anti-VEGF Adverse Events: Systemic adverse events including non-ocular haemorrhages and arterial thromboembolic events have been reported following intravitreal injection of VEGF inhibitors and there is a theoretical risk that these may relate to VEGF inhibition. There is limited data on safety in the treatment of patients with prior history of stroke or transient ischaemic attacks or myocardial infarction within the last 6 months.[7] See SPC for other adverse events. If clinically appropriate, SWL commission **ONE** switch to alternative anti-VEGF if first anti-VEGF had to be stopped due to an adverse event (either before efficacy could be assessed (i.e. before 3 consecutive monthly injections) or in patients who are responding to first anti-VEGF treatment).
Note 5 – Ranibizumab: One injection/month until max visual acuity (VA) is achieved and/or no signs of disease activity i.e. no change in VA and in other signs and symptoms of the disease under continued treatment (3 or more monthly injections may be needed). Thereafter, monitoring and treatment intervals should be determined by the physician and should be based on disease activity, as assessed by VA and/or anatomical parameters. For treat-and-extend regimen, once max VA is achieved and/or no signs of disease activity, treatment intervals can be extended stepwise by up to one month at a time until signs of disease activity or visual impairment recur. If disease activity recurs, the treatment interval should be shortened accordingly.[5,6] In clinical practice ranibizumab can be administered with or after laser photocoagulation.[16,17] SWL commission max 13 injections / year.
Note 6 – Aflibercept: One injection/month for 5 consecutive doses, followed by 1 injection every 2 months. There is no requirement for monitoring between injections. After 12 months and based on visual and/or anatomic outcomes, the treatment interval may be extended (treat-and-extend regimen); there are insufficient data to conclude on the length of these intervals. If visual and/or anatomic outcomes deteriorate, the treatment interval should be shortened accordingly. Monitoring intervals should be determined by the physician.[7] DRCR.net Protocol T showed that aflibercept and ranibizumab produced similar outcomes for eyes with better vision, whilst outcomes for those with worse vision (≤6/12 or ≤75 ETDRS letters) were more favourable with aflibercept.[18] SWL commission max 9 injection in year 1 and max 6 injections in subsequent years.
Note 7 – Faricimab: One injection/month for 4 consecutive doses, followed by treat-and-extend regime, using 4 weekly increments up to every 16 weeks. If visual and/or anatomic outcomes change, treatment intervals should be adjusted accordingly and interval reductions of up to 8 weeks may be implemented if deemed necessary.[9] FARETINA-DME showed faricimab treatment can be extended to intervals of 6 weeks and greater after the first two injections, with favourable outcomes in BCVA improvement and OCT reduction.[24,25] SWL commission max 13 injections / year.

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Note 8 – Brolucizumab: One injection/6 weeks for 5 consecutive doses. Thereafter, individualise treatment intervals based on disease activity as assessed by VA and/or anatomical parameters. In patients without disease activity, treatment every 3 months should be considered. In patients with disease activity, treatment every 2 months should be considered. Due to adverse event of intraocular inflammation, maintenance doses should not be less than 8 weeks apart.[8] Brolucizumab has been shown to be non-inferior to aflibercept.[26,27]
SWL commission max 8 injections in year 1 and max 6 injections in subsequent years.

Note 9 – Dexamethasone Intravitreal Implant: One implant. 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 DMO. There is no experience of the efficacy or safety of repeat administration beyond 7 implants.[19]
The summary of product characteristics states: "The safety and efficacy of Ozurdex® administered to both eyes concurrently have not been studied. Therefore administration to both eyes concurrently is not recommended." Any consideration of administration in both eyes is therefore at the discretion of the clinician after careful consideration of risks/ benefits.
Treatment is recommended for non-responders to non-corticosteroid treatment or those for whom it is unsuitable, irrespective of patient having an intraocular (pseudophakic) lens or natural (phakic) lens.[21] Dexamethasone may be preferred over anti-VEGF if prior history of stroke or transient ischaemic attacks or myocardial infarction within the last 6 months.[7]
SWL commission max 3 implants/eye/year until discontinuation indicated.[20] SWL have agreed that dexamethasone implant can be inserted at the time of cataract surgery.[14] Use in combination with anti-VEGF in the same eye is not routinely commissioned.

Note 10 – Switch Back From Dexamethasone to Anti-VEGF: This is commissioned if patient did benefit from anti-VEGF and was switched to dexamethasone due to high injection burden **or** cardiovascular events while on anti-VEGF therapy **or** vitrectomy **or** patients for whom anti-VEGF therapy was deemed unsuitable (e.g. due to other co-morbidities requiring frequent hospital appointments) **and**:

- patient did not benefit from dexamethasone **or**
- spike in IOP 60 days post dexamethasone implant[22] (observed after the first implant and if re-challenged with a subsequent implant) which does not revert to near baseline with careful therapeutic management.

A switch back from dexamethasone to anti-VEGF is **not commissioned** if there was no benefit on anti-VEGF treatment (i.e. stabilised or improved visual acuity **and/or** stabilised or reduced retinal thickness or improvement in other anatomical parameters if VA and CRT deteriorated).

Note 11 – Fluocinolone Intravitreal Implant: One implant. 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 DMO. Retreatments should not be administered unless the potential benefits outweigh the risks. Administration in both eyes concurrently has not been studied and is not recommended at the same visit. Concurrent treatment in both eyes is not recommended until the patient's systemic and ocular response to the 1st implant is known.[23] Implant can be used irrespective of patient having an intraocular (pseudophakic) lens or natural (phakic) lens.[28]
SWL commission max 2 implants / eye. Use in combination with ant-VEGF in the same eye is not routinely commissioned.

Note 12 – IFR: Funding requests for treatment outside this commissioned pathway can be made via the Individual Funding Request (IFR) process to the relevant commissioning organisation (see https://swlimo.southwestlondon.icb.nhs.uk/ for IFR policy and application form).

Refer to the relevant technology appraisal for each drug for further information about their eligibility and prescription.

SWL Drug Pathway - Diabetic Macular Oedema Drug Pathway: Drug information for advanced therapies

Version 2.1 (this list is not exhaustive; see summary of product characteristics (SPC) for full information)

Drug Class	Drug Name (Dose)	Administration	Contra-indications	Special warnings and precautions	
Anti VEGF	Ranibizumab (0.5mg) Faricimab (6mg) Aflibercept (2mg) Brolucizumab (6mg)	Intravitreal route	• Ocular or peri-ocular infection • Severe intra-ocular inflammation • Signs of irreversible ischaemic visual function loss in patients with retina vein occlusion • Hypersensitivity to the active substance or to any of the excipients	• Females of childbearing potential to use contraception during treatment and at least 3 months after last dose • Glaucoma (poorly controlled; do not use if intra-ocular pressure is ≥30 mmHg) • Intra-ocular surgery within the previous or next 28 days • Retinal detachment or macular hole (discontinue treatment if rhegmatogenous retinal detachment, retinal break, or stage 3 or 4 macular holes develop, until repaired) • Risk factors for retinal pigment epithelial tear • History of myocardial infarction, stroke, TIAs • Previous intravitreal injections • Arterial thromboembolic events and non-ocular haemorrhage	• Aneurysm and artery dissection in patients with or without hypertension • Any modifiable risk factors (such as smoking and hypertension) should be reduced as much as possible. Patients should be monitored and treated for hypertension as required. • Active systemic infection • Diabetic macular oedema due to type 1 diabetes (limited information available) • Diabetic patients with HbA1c over 12% (limited information available) • **Brolucizumab only:** intraocular inflammation and retinal vascular occlusive events occurred more frequently in the brolucizumab 3mg and 6mg groups than with the comparator 2mg aflibercept
Corticosteroid	Dexamethasone (700mcg)	Intravitreal route	• Active or suspected ocular or periocular infection (i.e. viral diseases of the cornea and conjunctiva, epithelial herpes simplex keratitis, vaccinia, varicella, mycobacterial infections, and fungal diseases) • Uncontrolled advanced glaucoma • Aphakic eyes with ruptured posterior lens capsule • Eyes with Anterior Chamber Intraocular Lens (ACIOL), iris or transscleral fixated intraocular lens and ruptured posterior lens capsule • Hypersensitivity to the active substance or to any of the excipients	• Elevated intraocular pressure • Cataract formation • Conjunctival or vitreal haemorrhage • Headache • Ocular hypertension, cataract subcapsular • Reduced visual acuity • Visual impairment/ disturbance • Vitreous detachment, floaters, opacities • Blepharitis	• Eye pain • Photopsia • Conjunctival oedema, hyperaemia • Endophthalmitis • Necrotizing retinitis • Retinal detachment and retinal tear
	Fluocinolone (190mcg)	Intravitreal route	• Active or suspected ocular or periocular infection (i.e. viral diseases of the cornea and conjunctiva, epithelial herpes simplex keratitis, vaccinia, varicella, mycobacterial infections, and fungal diseases) • Pre-existing glaucoma • Infectious uveitis • Hypersensitivity to the active substance or to any of the excipients	• Cataract formation • Increased intraocular pressure • Glaucoma • Retinal detachment • Optic disc haemorrhage • Conjunctival or vitreous haemorrhage • Reduced visual acuity • Visual field defect • Macula fibrosis • Blurred vision	• Hypotony of eye • Vitreous floaters, opacities • Foreign body sensation in eyes • Dry eye • Photopsia • Eye pain • Trabeculectomy, • Vitrectomy, trabeculoplasty

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SWL Drug Pathway - Diabetic Macular Oedema Drug Pathway: Version control

Version 2.1 (based on NICE with local adaptations)

Version number	Main amendments	Approval date
0	NICE TA274, TA301, TA346 and TA349	22 Jul 2015
1.0	Include approved recommendations from South West London Ophthalmology Medicines Optimisation network meeting (13th March 2020) including: • Local agreement on sequential treatment and switching between treatments • Local agreement for phakic women during conception/pregnancy • Local agreement on sequential use of fluocinolone if requiring frequent dexamethasone implants	15 Dec 2021
2.0	• Incorporate faricimab (NICE TA799), brolucizumab (NICE TA820) and dexamethasone (NICE TA824) into pathway • Add drug information for advanced therapies • Update format	20 Mar 2024
2.1	• Incorporate Fluocinolone acetonide (TA953) • Due to an administrative error, version 2.0 of the DMO pathway was not uploaded to the SWL IMO clinical guidance website	12 Apr 2024
Date of next review: 20 03 2026 (or earlier if indicated)		