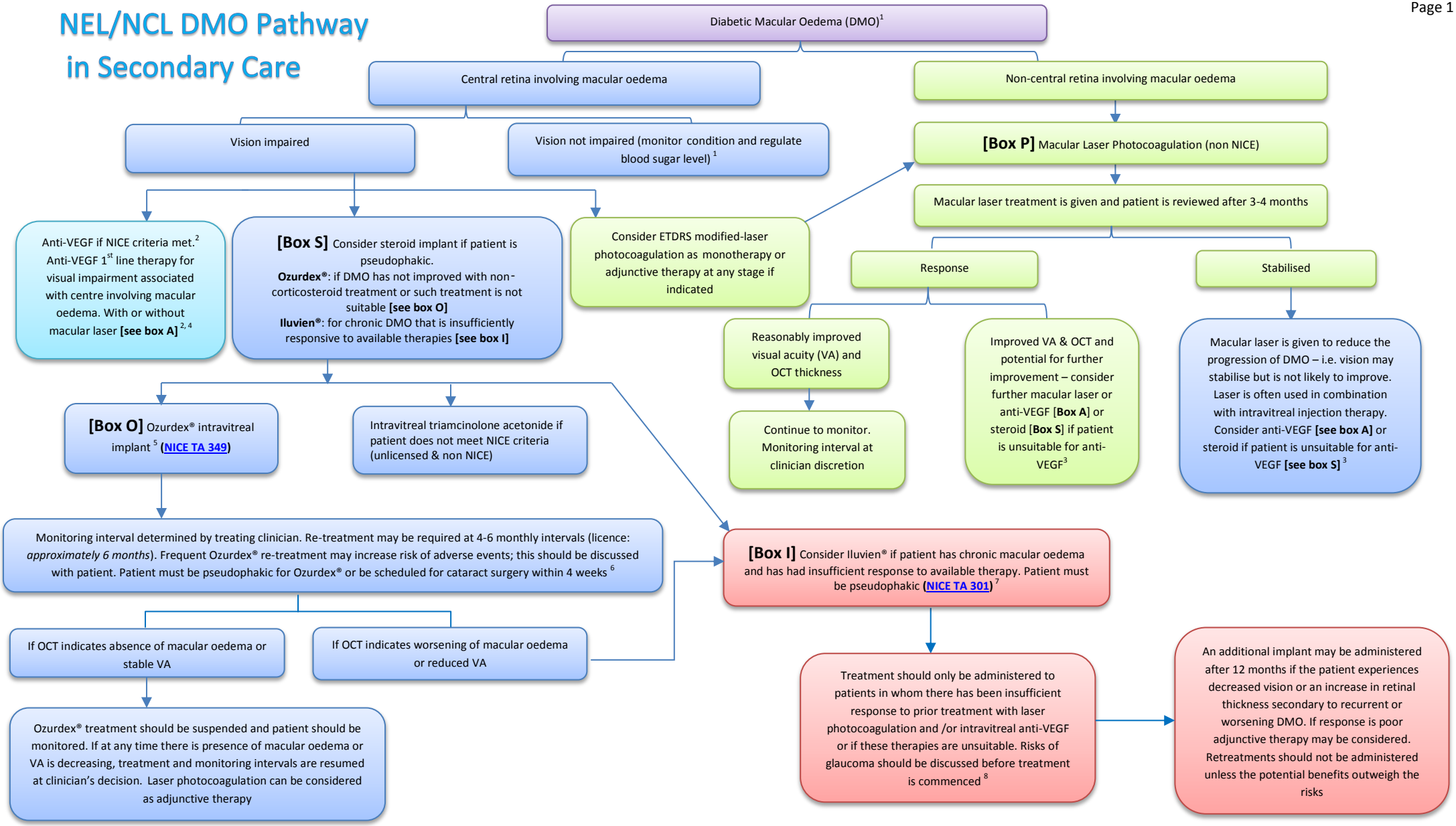
NEL/NCL DMO Pathway in Secondary Care



1 Check the level of glycated haemoglobin (HbA1c), blood pressure and lipid and if possible try to improve control before DMO therapy. OCT, FFA, DR Grade and treat proliferative retinopathy and/or severe peripheral ischaemic diabetic retinopathy if indicated
2 If no contra indication, no severe macular ischaemia, patient is symptomatic and wants treatment, discuss options: Conservative: Improve diabetes and review and/or macular laser treatment and/or intravitreal anti-VEGF
3 Patients with recent stroke or myocardial infarction (MI) or have a high risk of stroke / MI
4 Anti-VEGF treatments are recommended as an option for treating visual impairment due to DMO only if the eye has a central retinal thickness of 400 micrometres or more at the start of the treatment
5 Ozurdex® is recommended as a possible treatment for people with sight problems caused by DMO if patient is pseudophakic and their DMO has not improved with non-corticosteroid treatment, or such treatment is not suitable for them
6 As inflammation is expected following cataract surgery – it was agreed that patients with DMO who are phakic may be treated with Ozurdex® up to 4 weeks prior to the date on which the surgery has been scheduled. The safety and efficacy of Ozurdex® administered to both eyes concurrently has not been studied. Concurrent treatment to both eyes is not recommended until the patient's systemic and ocular response to the first implant is known (Ozurdex® SmPC)
7 Iluvien® is recommended as an option for treating chronic DMO that is insufficiently responsive to available therapies only if the implant is to be used in the eye with an intraocular (pseudophakic) lens
8 The safety and efficacy of Iluvien® administered to both eyes concurrently have not been studied. Concurrent treatment to both eyes is not recommended until the patient's systemic and ocular response to the first implant is known (Iluvien® SmPC)

[BOX A] Anti-VEGF if NICE criteria met [4, 12]
(eye has a central retinal thickness of ≥400 micrometres at the start of treatment)

[Box L] Lucentis® (NICE TA 274)

Treatment is given monthly until maximum VA and minimal OCT thickness are achieved under continued treatment then Lucentis® treatment is suspended (i.e. in practice is to treat until stable- improvements in vision, VA and OCT thickness is stable for the last 2 visits). Thereafter monitoring and treatment interval (not less than 4 weekly) should be determined by treating clinician based on VA and OCT thickness) [9, 11]

Treatment should be resumed if macular oedema increased and/or reduced vision (as assessed by VA and/or OCT thickness). The monitoring and treatment interval should be determined by treating clinician. Consider laser photocoagulation as adjunctive therapy

If VA, OCT thickness and no visual benefit indicate that the patient is not benefiting from continued treatment of Lucentis® despite a maximally appropriate course of therapy

[Box E] Eylea® (NICE TA 346)

Treatment is initiated with one injection per month for five consecutive doses, followed by one injection every two months. There is no requirement for monitoring between injections. After the first 12 months of treatment with Eylea®, the treatment interval may be extended based on visual and/or anatomic outcomes. The schedule for monitoring should be determined by the treating physician

OCT fluid increased or VA decreased

OCT fluid decreased or VA increased

Reduce treatment interval (minimum four weekly [unlicensed]) and consider laser photocoagulation as adjunctive therapy

Treatment and monitoring interval can be extended and should be determined by treating clinician based on visual and/or anatomic outcomes

OCT fluid increased or VA decreased

Insufficient response on 4 weekly dosing

If visual and anatomic outcomes indicate patient is not benefiting from continued treatment, Eylea® should be discontinued

Consider switch to alternative anti-VEGF [10, 11] **[Box E or L]** or steroid treatment if NICE criteria met (refer to page 1)

Box letter key	**Abbreviations**
P: Laser Photocoagulation	DMO: Diabetic macular oedema
A: Anti-VEGF	OCT: Ocular coherence tomography
E: Eylea® (Aflibercept)	VA: Visual acuity
L: Lucentis® (Ranibizumab)	ETDRS: Early treatment diabetic retinopathy study
S: Steroid	VEGF: Vascular endothelial growth factor
F: Iluvien® (Fluocinolone)	
O: Ozurdex® (Dexamethasone)	

Evidence for off label use

Ozurdex® 4 – 6 monthly dosing
- BEVORDEX study
- Ozurdex MEAD study
- Ozurdex PLACID study

Eylea® 4 weekly dosing
- Protocol T (DRCR.net) - Aflibercept, Bevacizumab and Ranibizumab Comparison for DME Study

Other references / further reading
- Intravitreal Aflibercept Injection in Diabetic Macular Edema Patients with and without Prior Anti-Vascular Endothelial Growth Factor Treatment: Outcomes from the Phase 3 Program. Ophthalmology. 2016 [Epub ahead of print]
- DRCR.net IVT Ranibizumab for DMO with Prompt versus Deferred Laser Treatment: 5-Year Randomized Trial Results. Ophthalmology. 2015 Feb;122(2):375-81
- Iluvien FAME study

9 Published data from the Diabetic Retinopathy Clinical Research Network shows that patients typically need 8 injections in Year 1, 3 injections in Year 2, 1 injection in Year 3 and ≤ 1 injection in Year 4 and 5
10 Maximum two switches between Eylea® and Lucentis® are allowed. Switching between Lucentis® and Eylea® is permitted for the purpose of attempting to reduce injection burden or improve visual outcomes
11 Re-loading of anti-VEGF would follow procedure as if switching has not occurred, e.g. if there had been a significant break in treatment or patient had not responded well in current anti-VEGF treatment, clinician may decide to re-load. If switching is due to attempt of reducing injection burden, reloading might not be applicable (outside scope of Eylea® / Lucentis® licence)
12 Both Eylea® and Lucentis® are NICE approved. NICE does not specify either agent as 1st or 2nd line, therefore both treatment options are presented to the patient. There may be a particular difference/advantage/disadvantage (i.e. treatment schedule) of a particular regime for specific patients; this will be explained to the patient

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