Macular Oedema secondary to Retinal Vein Occlusion (RVO)
SWL Drug Pathway

Version 1.0 (based on NICE with local adaptations)

Branch Retinal Vein Occlusion (BRVO)

Yes

Is vision impaired?

Yes

Central Retinal Vein Occlusion (CRVO)

Step 1:
- Aflibercept (TA409) (note 3)

Laser photocoagulation
Unless not suitable because of extent of macular haemorrhage

Yes-maintain treatment as per SPC (note 3)

Is there evidence of response to treatment i.e.
- Reduction in retinal thickness and/or dry macula on OCT with improvement in VA by at least 5 letters compared to baseline? OR
- Reduction in retinal thickness and/or dry macula with stabilisation of VA (no deterioration) compared to baseline?

(Use ETDRS letter chart in which 85 letters = 6/6)

No

Laser photocoagulation
Unless not suitable because of extent of macular haemorrhage or previously unsuccessful

Step 2: Dexamethasone (TA229) (note 4,8)

Yes-maintain treatment as per SPC (note 4)

Is there evidence of response to treatment i.e.
- Reduction in retinal thickness and/or dry macula on OCT with improvement in VA by at least 5 letters compared to baseline? OR
- Reduction in retinal thickness and/or dry macula on OCT with stabilisation of VA (no deterioration) compared to baseline?

(Use ETDRS letter chart in which 85 letters = 6/6)

Note for Dexamethasone: if spikes in intra-ocular pressure after max 2 implants, which does not revert to near baseline with careful therapeutic management, consider switch back to anti-VEGF if patient benefitted from anti-VEGF but was switched to dexamethasone due to high injection burden **or** cardiovascular events while on anti-VEGF therapy **or** vitrectomy (note 7).

No

Step 1:
- Dexamethasone (TA229) (note 1,4,8) consider if recent cardiovascular events; those who do not favour monthly injections, if affected eye vitrectomised or during conception and pregnancy **or**
- Anti-VEGF: **1st choice:** Ranibizumab (TA283) (note 1,2,6) **or** **2nd choice:** Aflibercept (TA305&409) (note 1,3,6)

Is there evidence of response to treatment i.e.
- Reduction in retinal thickness and/or dry macula on OCT with improvement in VA by at least 5 letters compared to baseline? OR
- Reduction in retinal thickness and/or dry macula on OCT with stabilisation of VA (no deterioration) compared to baseline?

(Use ETDRS letter chart in which 85 letters = 6/6)

Yes-maintain same treatment as per SPC (note 2,3,4) or consider switch from ranibizumab to aflibercept (note 5)

No

Step 2: Switch to alternative drug class:
- Dexamethasone (TA229) (note 4,) **or**
- Anti-VEGF: **1st choice:** Ranibizumab (TA283) (note 1,2,6) **or** **2nd choice:** Aflibercept (TA305&409) (note 1,3,6)

Is there evidence of response to treatment i.e.
- Reduction in retinal thickness and/or dry macula on OCT with improvement in VA by at least 5 letters compared to baseline? OR
- Reduction in retinal thickness and/or dry macula on OCT with stabilisation of VA (no deterioration) compared to baseline?

(Use ETDRS letter chart in which 85 letters = 6/6)

Note for Dexamethasone: if spikes in intra-ocular pressure after max 2 implants, which does not revert to near baseline with careful therapeutic management, consider switch back to anti-VEGF if patient benefitted from anti-VEGF but was switched to dexamethasone due to high injection burden **or** cardiovascular events while on anti-VEGF therapy **or** vitrectomy (note 7).

Yes-maintain same treatment as per SPC (note 2,3,4) or consider switch from ranibizumab to aflibercept (note 5)

No

No

Discontinue high cost drug treatment (note 9)

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Clinicians and commissioners should refer to the relevant technology appraisal and SPC for each drug for further information about eligibility and prescription

Note 1- 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 should be considered as a 1st choice anti-VEGF option due to anticipated biosimilar savings in the near future.

Note 2- Ranibizumab: One injection/month until maximum visual acuity is achieved and/or there are no signs of disease activity i.e. no change in visual acuity and in other signs and symptoms of the disease under continued treatment. In patients with RVO, initially, three or more consecutive, 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 may be gradually extended, however there are insufficient data to conclude on the length of these intervals. If disease activity recurs, the treatment interval should be shortened accordingly.[1] SWL commission max 12 injections/year (per eye).

1. www.medicines.org.uk Lucentis SPC accessed 31/03/2020; SPC last updated 08/07/2019

Note 3- Aflibercept: One injection/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. Treatment may then be continued with a treat-and-extend regimen with gradually increased treatment intervals to maintain stable visual and/or anatomic outcomes, however 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. The monitoring and treatment schedule should be determined by the treating physician based on the individual patient's response. Monitoring for disease activity may include clinical examination, functional testing or imaging techniques (e.g. optical coherence tomography or fluorescein angiography).[1] SWL commission max 12 injections/year (per eye).

1. www.medicines.org.uk Eylea SPC accessed 31/03/2020; SPC last updated 08/07/2019

Note 4- Dexamethasone intravitreal implant: One implant. Administration to both eyes concurrently is not recommended. 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 OZURDEX, should not be retreated. There is only very limited information on repeat dosing intervals less than 6 months. Patients should be monitored following the injection to permit early treatment if an infection or increased intraocular pressure occurs.[1]
NICE TA 229 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."[2]
Dexamethasone may be preferred:

- if prior history of stroke or transient ischaemic attacks or myocardial infarction within the last 6 months[4,5]
- in vitrectomised eyes[6]
- if patients do not favour frequent injections[5]
- during conception and pregnancy (due to potential teratogenic and embryo-foetal toxicity of anti-VEGFs)[1]

SWL commission max 3 implants / eye / year until discontinuation indicated.[3] Use in combination with ant-VEGF in the same eye is not routinely commissioned.

1. www.medicines.org.uk Ozurdex SPC accessed 31/03/2020; SPC last updated 24/10/2019
2. NICE TA229 section 4.11
3. Malclès A, *et al.* Safety of intravitreal dexamethasone implant (Ozurdex): The SAFODEX study. Incidence and risk factors of ocular hypertension. Retina 2017; 37(7): 1352-1359
4. www.medicines.org.uk SPC accessed 31/03/2020; SPC last updated 07/01/2020 (Lucentis)/08/07/2019 (Aflibercept).
5. The Royal College of Ophthalmologists. Retinal Vein Occlusion (RVO) guidelines. July 2015
6. Chang-Lin J *et al.* Pharmacokinetics of a sustained-release dexamethasone intravitreal implant in vitrectomized and nonvitrectomized eyes. Invest Ophthalmol Vis Sci 2011:52:4605-4609
7. www.medicines.org.uk SPC accessed 31/03/2020; SPC last updated 07/01/2020 (Lucentis)/08/07/2019 (Eylea)

Note 5- Sequential anti-VEGF treatment: There is very limited evidence for switching anti-VEGFs in RVO. SWL commission one switch from ranibizumab to aflibercept if switch is considered for one of the following reasons[1]:

- High injection frequency with ranibizumab[2]
- Worsening or new peripheral ischaemia (aflibercept trials included 32% of patients with a mix of ischaemia /intermediate ischaemic eyes[3,4] whereas ranibizumab trials excluded all ischaemic patients via the brisk afferent pupillary defect (RAPD) test[5])
- Progression to vascular DMO[6]

1. Local clinical expertise
2. Eadie JA *et al.* Response to aflibercept as secondary therapy in patients with persistent retinal edema due to central retinal vein occlusion initially treated with bevacizumab or ranibizumab. Retina 2014; 0:1-5
3. Heier JS *et al. Intravitreal aflibercept injection for macular edema due to central retinal vein occlusion. Two-year results from the COPERNICUS study. Ophthalmol 2014; 121:1414-1420*
4. Korobelnik J *et al.* Intravitreal aflibercept injection for macular edema resulting from central retinal vein occlusion. One-year results of the phase 3 GALILEO study. Ophthalmol. 2014; 121: 202-208
5. Brown DM *et al. for CRUISE investigators.* Ranibizumab for macular edema following central retinal vein occlusion. Six-month primary end-point results of a Phase III study. Ophthalmol 2010; 117(6): 1124-1133.
6. Local clinical expertise

Note 6- 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.[1] 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).

1. www.medicines.org.uk SPC accessed 31/03/2020; SPC last updated 07/01/2020 (Lucentis)/08/07/2019 (Eylea)

Note 7- Switch back from dexamethasone to anti-VEGF: SWL commission a switch back from dexamethasone to original anti-VEGF, or to aflibercept if patient was on ranibizumab before (see note 4), 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 **and**:

- patient did not benefit from dexamethasone **or**
- spike in IOP 60 days post dexamethasone implant[1] (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 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).

1. Haller JA *et al. for the* Ozurdex GENEVA Study Group. Randomised, sham-controlled trial of dexamethasone intravitreal implant in patients with macular edema due to retinal vein occlusion. Ophthalmology 2010; 117:1134-1146

Note 8- Pregnancy: Following careful consideration of expected benefits/risks of all treatment options, SWL allow a switch to dexamethasone in women meeting NICE criteria during conception and pregnancy (due to potential teratogenic and embryo-foetal toxicity of anti-VEGFs[1]) followed by a switch back from dexamethasone to anti-VEGF after the pregnancy if patient did benefit from anti-VEGF.

1. www.medicines.org.uk SPC accessed 31/03/2020; SPC last updated 07/01/2020 (Lucentis)/08/07/2019 (Eylea)

Note 9- Funding requests for treatment outside this commissioned pathway can be made via the Individual Funding Request (IFR) processto the relevant commissioning organisation (see www.swlmcg.nhs.uk for IFR policy and application form).

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Version number	Main amendments	Approval date
0	NICE TA229, TA283, TA305 and TA409	28 Sep 2016
1.0	Include approved recommendations from South West London Ophthalmology Medicines Optimisation network meeting (13th March 2020) including: • Local agreement on drug choices • Local agreement on sequential treatment and switching between treatments • Local agreement for women during conception/pregnancy • Define patient groups who would benefit from dexamethasone in step 1	15 Dec 2021
Date of next review: December 2025 (or earlier if indicated)		