Macular degeneration

Consultation on draft guideline – deadline for comments 5pm on 24th August 2017 **email: MacularDegeneration@nice.org.uk**

	Please read the checklist for submitting comments at the end of this form. We cannot accept forms that are not filled in correctly. We would like to hear your views on the draft recommendations presented in the short version and any comments you may have on the evidence presented in the full version. We would also welcome views on the Equality Impact Assessment. We would like to hear your views on these questions: 1. Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why. 2. Would implementation of any of the draft recommendations have significant cost implications? 3. What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.) 4. [Insert any specific questions about the recommendations from the Developer, or delete if not needed] See section 3.9 of Developing NICE guidance: how to get involved for suggestions of general points to think about when commenting.
Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	The Royal College of Ophthalmologists

NICE National Institute for Health and Care Excellence

Consultation on draft guideline – deadline for comments 5pm on 24th August 2017 **email:** **MacularDegeneration@nice.org.uk**

Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	N/A

Macular degeneration

Consultation on draft guideline – deadline for comments 5pm on 24th August 2017 **email:** **MacularDegeneration@nice.org.uk**

Name of commentator person completing form:	Professor Andrew Lotery, Chair of the Scientific Committee Professor Andrew Lotery, Chair of the Scientific Committee Contributions from Professor Andrew Lotery, Consultant Ophthalmologist and Chair of the Scientific Committee (RCOphth) Mr Augusto Azuara-Blanco, Consultant Ophthalmologist Professor Usha Chakravarthy, Consultant Ophthalmologist Mr Michael Burdon, Consultant Ophthalmologist and President (RCOphth) Miss Melanie Hingorani, Consultant Ophthalmologist and Chair of the Professional Standards Committee (RCOphth) Mrs Kathy Evans, Chief Executive of the RCOphth Professor Caroline MacEwen and Ms Alison Davis, Consultant Ophthalmologists and Co-leads for the Ophthalmology Getting it Right First Time project Mr Ian Pearce, Consultant Ophthalmologist Mr James Talks, Consultant Ophthalmologist

Macular degeneration

NICE National Institute for Health and Care Excellence

Consultation on draft guideline – deadline for comments 5pm on 24th August 2017 **email:** MacularDegeneration@nice.org.uk

Type		[office use only]		
Comment number	**Document** (**full** version, **short** version or the **appendices**	**Page number** Or **'general'** for comments on the whole document	**Line number** Or **'general'** for comments on the whole document	**Comments** Insert each comment in a new row. Do not paste other tables into this table, because your comments could get lost – type directly into this table.
Example 1	Full	16	45	We are concerned that this recommendation may imply that ……..
Example 2	Full	16	45	Question 1: This recommendation will be a challenging change in practice because ……
Example 3	Full	16	45	Question 3: Our trust has had experience of implementing this approach and would be willing to submit its experiences to the NICE shared learning database. Contact……..
1	Overall comment		general	Overall the RCOphth supports this guideline and agrees the recommendations will have a positive impact in delivering care for people with AMD. It would be useful to have Figures with algorithms to describe decision making and patients' pathways For wet active AMD: the impact of repeated intraocular injections of antiagiogenic therapies and

				frequent visits to hospital eye services in quality of life (QoL) have not been considered. Quantification of "disutilities" associated with repeated intraocular injections of anti-angiogenic therapies and hospital visits would perhaps be a useful research recommendation.
2	short version	Section 1.4.11	7-11	The recommendation should be explicit about the need for a clear urgent referral pathway and include an associated requirement to educate and support those in primary care to identify suitable patients and be able to use that pathway.
3	Short version	4	Definitions in table	Adult vitelliform lesion is a confusing term. Adult vitelliform dystrophy is a different condition from AMD. This term should not be used. Indeterminate AMD – see comment below.
4	Short version	7	Section 1.4.2	Subtle features such as sub-retinal fluid, intra-retinal fluid other pathology eg vitreomacular traction can all be missed by slit-lamp examination alone. It is not clear why OCT is being excluded as a diagnostic test. It is the practice of almost all medical retinal specialists to use OCT imaging in clinical practice for AMD including early or late dry AMD. Increasingly high street optometrists have this technology too so it should not be recommended to just use slit lamp examination when OCT is so useful and widely available.
5	Short version	7	Section 1.4.5	Dry AMD patients should also be referred to hospital so they can participate in clinical trials which are becoming increasingly widely available.
6	Full guideline short version	Sections 7.1 and 7.2 pages 75-93 1.4.8 and 1.4.9 pages 7-8	general	**(1) diagnostic tests to detect early AMD and late dry AMD:** suggest fundus auto-fluorescence should be considered as a potentially useful diagnostic test to include in the review, as it detects and quantifies atrophy of the retinal pigment epithelium. **(2) Choice of reference standard to diagnose wet active AMD** The reference standard should be the best test currently available, and is the standard against which the index test is compared. It need not be the test used routinely in practice (although it can be). It is unclear why the committee used two different reference standards to diagnose wet AMD. In section 7.1. the reference standard used was fluorescein angiography, FFA. However, in section 7.2 the reference standard was OCT (and FFA was considered to be an index test). It is unclear why a

				different reference standard has been used. The RCOphth suggests the reference standard for diagnosing wet AMD should be FFA (as used in Section 7.1) and not OCT.
7	Full guideline short version	Section 7.2 pages 80 -93 1.4.8 and 1.4.9 pages 7-8	general	There is an attempt to validate the selection of OCT as reference standard to diagnose wet AMD in section 7.2.4., **Page 89: "the committee noted at the largest, most recent, UK-based study co compare OCT with FFA (Wilde et al, 2015) found no false-negative diagnosis at all (a sensitivity of 100%) but was subject to a false positive rate of around 1-in-5 (specificity of 81%). The committee agree that these findings provided good validation of the current common practice of using OCT as a non-invasive first-line investigation, to rule out cases that do not have late AMD (wet active), in identify those that require FFA to confirm a positive diagnosis".** However: there is no mention of high risk of bias of the paper by Wilde et al.; this study is retrospective, and excluded 346 of 822 (42%) potential participants and thus not generalisable. There was no detailed explanation of reasons of exclusion (i.e., whether it was due to OCT or FFA or both tests). In addition, the reported sensitivity was not 100% because for one participant with wet AMD the OCT was interpreted as negative (page 606) and only after knowing the result of the FFA the OCT test was re-classified.
8	Full guideline short version	Section 7.2 pages 80 -93 1.4.8 and 1.4.9 pages 7-8	general	**(3) Section 7.2.4. Evidence to recommendation section. Pages 90-92, Considerations of health benefits and resource use:** **"The committee considered that the modelled cohort in the included CUA had some characteristics that are not representative of the group's clinical experience. In particular the committee considered 6/24 as an upper bound for presenting VA as an unrealistic assumption, given that many patients will present with greater loss of vision".** Incorporating people with very poor visual acuity would mean that only a small QALY difference would be possible and thus the least costly strategy would be selected in the CUA (a cost-minimisation approach) **"The assumption that 10% of patients will receive FFA was also considered too conservative and… it was agreed that this would underestimate the total cost of FFA"** Higher uncertain results of other diagnostic tests would reduce their relative cost-effectiveness. This

				was tested in sensitivity analysis with the unclear results from the Ophthalmologist or nurse assessments rising to 50% ad no unclear test results from OCT. While Ophthalmologist or nurse led assessment were less cost-effective, OCT only based diagnosis was still being dominated by FFA-based diagnosis. **"The committee also considered that the cost of treatment in the model did not reflect the patient access scheme pricing for ranibizumab, and that the model could have considered other treatment options in a scenario analysis"** The committee seems to ignore the scenario analysis conducted with details provided in page 71, including a cost for anti-VEGF therapy of £50. "Scenario analysis was conducted in order to explore the conditions under which an OCT only strategy would become cost-effective…" **"The parameterised diagnostic accuracy of OCT was also considered to be a likely underestimate of the current state-of-the-art as image resolution has improved considerably since the studies in the authors' systematic review were published"** It is unclear how much the diagnostic decisions can be improved with improved technology. E.g., recent studies reporting diagnostic performance of OCT-A for wet active AMD have been considered to be of poor quality by the committee. **"On examining the diagnostic accuracy parameters, the committee agreed it was a weakness of the model that a systematic review was undertaken to establish sensitivity and specificity ranges for OCT, but that the 'Ophthalmologist' diagnostic strategy, which includes OCT, is based entirely on expert opinion. There are evidently correlations between strategies that share a common diagnostic tool and his is not accounted for in the model. Given the assumption of perfect information for FFA, and an expert opinion based parameterisation of the 'Ophthalmology' strategy, the committee felt that the model could be systematically biased away from OCT."** We agree that correlations would have an impact in the probabilistic analysis. However, the bias would be in favour of OCT only strategies. If positive correlations were allowed for, higher (lower) sensitivity and specificity from the possible range would favour results for ophthalmologist or nurse

				strategies each time a high (low) value was sampled for OCT only. **"The committee also agreed that important differences between the invasiveness of FFA and OCT had not been accounted for in the model"** We do not think FFA has a significant impact in QoL.
9	Short version	8	14-16	It would be useful to specify the type of anti-VEGF that is currently recommended, i.e., "offer ranibizumab or aflibercept"
10	Short version	8	Section 1.5.2	This section contradicts previous NICE guidance that treatment should not be given if visual acuity is worse than 6/96. Do you mean use bevacizumab in this scenario where NICE states not to use ranibizumab or aflibercept. Please clarify as the current statement is contradictory and ambiguous.
	Short Version	8	26	The statement "Bevacizumab is not licensed for intraocular use for AMD" is factually correct. The 2014 RCOphth public statement on Bevacizumab concluded with "There is clear evidence that, despite the lack of a licence, Avastin is a safe and effective drug for the treatment of neovascular AMD. The College would therefore welcome an urgent review of this issue by the United Kingdom Health Regulatory Bodies to consider how this unusual situation can be remedied". https://www.rcophth.ac.uk/2014/12/use-of-avastin-bevacizumab-in-age-related-macular-degeneration-2/ This remains our position.
11	Short Version	9	10-13	Treatment via intravitreal injections are cost effective from 6/12-6/96. There are clear benefits shown in the following paper that treating patients with AMD with VA better than 6/12. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4431059/. Why is only Ranibizumab recommended? NICE did show benefits for Bevacizumab in VA better than 6/12 which is where there are benefits for CCG's and the NHS as a whole. It is estimated that about a third of new patients could be treated if treatment started at better than

				6/12. Every patient will lose vision and hit the 6/12 mark the recommendation to delay treatment until vision has reduced to this level means patients will lose sight unnecessarily. Starting treatment at an earlier stage would significantly reduce costs (in the order of millions of pounds) to the whole NHS system as these patients' vision would then be maintained at a higher level. Bevacizumab is as efficacious as Ranibizumab. There are two studies which confirm this (CATT and IVAN). These studies were mentioned in the RCOphth letter to the GMC in 2015. There is no direct RCT head to head comparison of Bevacizumab to Aflibercept. However, it can be extrapolated that as aflibercept = Ranibizumab then they are likely to be equally efficacious. The RCOphth calls for clinicians to be able to use their judgement to prescribe Bevacizumab for patients with VA better than 6/12 when appropriate. To provide the most clinically and cost effective care to patients, clinicians should have access to Bevacizumab as a first line treatment with the ability to switch to another drug (licenced) at their clinical discretion. Clinicians should also have access to Bevacizumab if there is a limited response to aflibercept and Ranibizumab. We accept there is no RCT data to support this, but in line with the above evidence this would be a pragmatic and cost effective approach. Clinicians should be able to use all tools in their armoury. This would be supported by GMC as failure of the other two drugs essentially means that clinicians have run out of licensed alternatives. Clinicians should also have access to bevacizumab where a licenced drug is not available eg Wet AMD with visual acuity better than 6/12 or worse than 6/96 or where the choroidal neovascularization falls outside current NICE guidance eg peripapillary or extra-foveal.
12	Short version	9-10	29-13	**1.5.7. and 1.5.8. Pegaptanib is not recommended for the treatment of wet age-related macular degeneration.** Perhaps people who are currently receiving pegaptanib should not have the option to continue therapy and should be switched to more effective anti-VEGF therapies.

13	Short version	11	1-5	**1.5.14. Switching antiangiogenic therapy**. It would be useful to specify that the comment regarding switching antiangiogenic therapy refers to ranibizumab and aflibercept.
14	Short version	12-13	2-12	The monitoring recommendation should include the need to ensure timely bookings and chase DNAs and cancellations is often used to ensure safe regular delivery of treatment in active disease.
15	Short version	13	Section 1.7.9	Autofluorescent imaging is also a very useful test to investigate a decline in visual acuity. It is much more sensitive than a colour photograph in detecting for example progression of foveal atrophy. This imaging modality should be included here and also in general in the guidelines.
16	Full version	28	3 (table)	Indeterminate is a new term, it is inappropriate. The distinction should be made by multimodal imaging to identify AMD mimics from non-AMD. There is nothing indeterminate about AMD. There are exudative macular lesions which are not AMD and ophthalmologists are able to differentiate these conditions from neovascular AMD. With the advent of OCT A and high resolution FA and ICG with OCT ophthalmologists can make these distinctions.
17	Full version	28	3 (table)	Atrophy. Evidence supports the view that depigmentation and GA are not distinguishable easily if diam is < 175. Retain this cut off. There appears to be some confusion regarding depigmentation and its distinction from GA. GA is a term that was used previously to distinguish an area of retina on clinical examination that appeared devoid of cellular components (photoreceptors/RPE and choriocapillaris). Now with multimodal imaging ophthalmologists can see incomplete atrophy in some layers giving rise to the depigmentation and fully developed GA where outer retina and RPE are lost and this is seen when the diameter of the lesion exceeds 150 microns and thus the 175 micron which the WARMGS classification suggested seems reasonable. Anything less than 175 should not be termed GA
18	Full version	46	3 Table 13: AMD classification	Evidence for use of PDT as combination for PCV is strong and growing stronger therefore the treatment algorithm is out of date.
19	Short version	page 9, line 10 to	1.5.5-1.5.8	This section perhaps inadvertently seems to favour ranibizumab over aflibercept for treatment of wet AMD. We recommend it is rephrased.

		page 10, line 19		The recommendation for ranibizumab is clearly stated (1.5.5), but the recommendation for aflibercept is only stated after recommending that pegaptanib shouldn't be used (1.5.6 & 1.5.7), and only in terms of a reference that is should be used in accordance with the recommendations for ranibizumab in NICE technology appraisal guidance 155. We think the positive recommendation to use aflibercept should immediately follow that for ranibizumab, and clearly state the criteria for use as is done in the second part of 1.5.5 for ranibizumab ("the best-corrected visual acuity is between 6/12 and 6/96 ...."). Failure to make these changes might lead to the suggestion that ranibizumab is favoured over aflibercept
20	Short version	Page 8	1.5.3	It says injections can be given by a practitioner with experience of injections. Clearly this should be qualified by appropriately trained and should be under the supervision of a qualified medical practitioner. Our patients are often elderly and could have a reaction or collapse so there needs to be suitable support available, secondly often such practitioners are also making decisions and they need to have ready access to appropriate advice and support.
21	Both versions	General		We would like to emphasise the increasing role of multimodal imaging in the mangagement of AMD which is downplayed in this document. Increasingly autofluorescence, OCT-A and multimodal imaging is used to properly diagnose patients for example some cases of GA may in fact be late on set Stargadts or LORD and so AF and a multi model approach to imaging is needed. MacTel can also be confused.
22	Both versions	General		The method of giving intravitreal injection, setting, procedure etc is not mentioned and should be. The Royal College of Ophthalmologists has previously published guidelines on this.

Insert extra rows as needed

Checklist for submitting comments

- Use this comment form and submit it as a Word document (not a PDF).
- Complete the disclosure about links with, or funding from, the tobacco industry.
- Include page and line number (not section number) of the text each comment is about.

Macular degeneration

NICE National Institute for Health and Care Excellence

Consultation on draft guideline – deadline for comments 5pm on 24th August 2017 **email: MacularDegeneration@nice.org.uk**

- Combine all comments from your organisation into 1 response. We cannot accept more than 1 response from each organisation.
- Do not paste other tables into this table – type directly into the table.
- Underline and highlight any confidential information or other material that you do not wish to be made public.
- Do not include medical information about yourself or another person from which you or the person could be identified.
- Spell out any abbreviations you use
- For copyright reasons, comment forms do not include attachments such as research articles, letters or leaflets (for copyright reasons). We return comments forms that have attachments without reading them. The stakeholder may resubmit the form without attachments, but it must be received by the deadline.

You can see any guidance that we have produced on topics related to this guideline by checking NICE Pathways.

Note: We reserve the right to summarise and edit comments received during consultations, or not to publish them at all, if we consider the comments are too long, or publication would be unlawful or otherwise inappropriate.

Comments received during our consultations are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the comments we received, and are not endorsed by NICE, its officers or advisory Committees.