National Institute for Health and Clinical Excellence

648 – Epiretinal brachytherapy for wet age related macular degeneration

Consultation Comments table

IPAC date: Thursday 9 September 2011 and 13 October 2011

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 The Macular Disease Society is a member of the MERLOT trial steering group.	**1**	We agree with this recommendation	Thank you for your comment.

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2	Conusultee 2 Manufacturer	**1.1**	I commented on the fact that 3 year data had been submitted for publication, and such data should be considered by the committee. I also highlighted the difference between our approach to treating both naïve disease and chronic disease as the expected outcome post-tx will likely be different in each group	Thank you for your comment. From the information available these data you make reference to are part of the CABERNET trial which is scheduled to be completed in August 2012. The Interventional Procedures Programme does not usually consider publication of interim study findings that have not undergone full peer-review, except where it reveals substantial and/or new safety concerns. In addition, when guidance about a procedure is issued with 'special arrangements' recommendations the guidance is considered for potential updating after 3 years – depending on the change in the evidence base. Similarly, such guidance (relating to special arrangements recommendation) could also considered for updating if the Programme is advised of the publication of safety or efficacy outcomes that can be judged to represent substantive changes in the evidence base.
3	Consultee 1 The Macular Disease Society is a member of the MERLOT trial steering group.	**2.1**	Patients with advanced disease may also benefit from training to help them identify alternative fixation points. This is called "eccentric viewing"	Thank you for your comment. Section 2.1.2 of the guidance will be changed.
4	Conusultee 2 Manufacturer	**2.2.2**	I Provided a more detailed explanation of the procedure [	Thank you for your comment. The description of the procedure in the guidance is aimed to provide a broad overview only. In subsequent correspondence it was agreed that the description is fair.

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5	Conusultee 2 Manufacturer	**2.2.3**	I disagreed with this statement, as there are no other devices, besides ours, for performing epiretinal brachytherapy	Thank you for your comment. The Committee was advised that epiretinal brachytherapy using different devices has been described and therefore it was not possible to change this section.
6	Conusultee 2 Manufacturer	**2.3.2**	Again, I called out the pending 36 month data	Thank you for your comment. Please see response to comment number 2.
7	Conusultee 2 Manufacturer	**2.3.2 cont**	For naïve disease, or de novo patients, we undertook a study utilizing our treatment with 2 injections of Avastin followed by further Avastin injections on an as needed basis. This study recently completed the third year of follow-up and has been published in a peer review journal. All 34 subjects were followed-up for 24 months and 19 were followed-up through 36 months. With up to 24 months of follow-up, 12 of 24 phakic patients (50%) exhibited ≥2 grades of progression in Lens Opacification Classification System (LOCS) II lens classification; 5 eyes underwent cataract extraction before the Month 36 visit. There was 1 case of nonproliferative retinopathy identified at 36 months of follow-up that did not have an adverse effect on visual acuity, was stable at 43 months of follow-up, and was isolated to the parafoveal region. Mean best-corrected visual acuity in this case demonstrated an average gain of +15.0 and 24.9 letters at 12 months and 24 months, respectively; the drop in mean gain at Month 24 was largely attributable to cataract	Thank you for your comment. The first of these two studies was provided and has been published in August 2011, soon after the updated literature search for the procedure was carried out (in late July). This Committee included this paper in its consideration of the evidence and this study will be included in the procedure Overview document and also in the Interventional Procedures document. The consultee has also offered additional currently unpublished data. The Interventional Procedures Programme does not usually consider unpublished (that has not as yet undergone peer review) , except where it reveals substantial and/or new safety concerns.

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			formation. At 36 months (n = 19), the mean best-corrected visual acuity was +3.9, 90% (17 of 19) of eyes had lost ,15 letters from baseline, 53% (10 of 19) had gained ≥1 letter, and 21% (4 of 19) had gained ≥15 letters. Through 36 months, 11 eyes required additional bevacizumab retreatment therapy and received a mean of 3.0 injections (range, 2–7 injections), and 8 eyes remained completely free of additional injections. For chronic disease, or for patients who require frequent Anti-VEGF injections to manage the disease, we undertook another study, that was designed with 2 primary endpoints – (1) Maintain vision while (2) Reducing the number of needed injections. The 12 month results from this study (n=53) have been submitted for publication – some of the top line results of this study are as follows: 1. Prior to enrollment, participants had received on average 12.3 anti-VEGF injections. 2. After a single treatment with 24 Gy beta radiation, 81% maintained stable vision, and 47% improved (>0 letters improvement), with a mean of 3.2 anti-VEGF retreatments in 12 months. 3. Mean (±SD) change in visual acuity was -4.0 (± 15.1 ETDRS letters). 4. Common adverse events included	

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			conjunctival hemorrhage, cataract, eye pain, and resolving vitreous hemorrhage, all of which can be attributed to the surgical vitrectomy procedure.	
8	Conusultee 2 Manufacturer	**2.4.4**	Again I referenced to coming 36 month data.	Thank you for your comment. See reply to comments 2 and 7.
9	Conusultee 2 Manufacturer	**2.4.4 cont**	I also argued against any consideration based on theory, as our approach is a much safer approach than any prior approaches for delivering a dose of radiation to the macula	Thank you for your comment. The specialist adviser safety section, lists the advice received on theoretical safety outcomes/concerns for each procedure. Identifying and listing such advice and commentary is integral to the methods and process of the Interventional Procedures Programme.
10	Conusultee 2 Manufacturer	**general**	Data from our primary Phase 3 clinical study, CABERNET, will be presented on October 21, during this year's American Academy of Ophthalmology. The CABERNET Study is the largest device trial ever conducted in Ophthalmology, with enrolment of 493 patients in 41 clinical sites throughout the world, including sites in the United Kingdom. I ask that you please consider delaying your Guidance Document on Epiretinal Brachytherapy until after the CABERNET Study data is released. By so doing, you and your colleagues will be provided a more thorough clinical review, thus permitting your team to author a more complete and accurate assessment of our procedure "	Thank you for your comment. The Interventional Procedures Programme does not usually consider publication of interim study findings that have not undergone full peer-review, except where it reveals substantial and/or new safety concerns. Please also see reply to comment 2.

understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees."