Comments on the ACD Received from the Public through the NICE Website

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	We agree with this recommendation as, based on the available information, this treatment would not be cost-effective use of NHS resources, compared to other treatment options for the same condition. Ranibizumab for the treatment of macular oedema secondary to RVO is not a cost effective use of NHS resources The Committee determined that the most plausible ICERs for ranibizumab compared with alternatives were all above the ranges usually considered cost-effective for NHS use (i.e. £20,000 to £30,000 per QALY gained).
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	The clinical trials that assessed the effectiveness of ranibizumab are not fully generalisable to NHS clinical practice. There is therefore a lack of evidence for the effectiveness of ranibizumab for treatment of RVO in patients with severe ischaemia. The outcomes in the trial of ranibizumab for branch retinal vein occlusion were confounded. In the BRAVO trial, patients were treated with monthly ranibizumab or sham injections for six months however, after three months the patients could receive grid laser photocoagulation for rescue treatment. This was used in 57.6% of patients in the sham injection group and 21.4% of the ranibizumab group in the first six months. It was noted that the treatment period of the BRAVO trial was insufficient to capture any benefits of grid laser photocoagulation on patient outcomes, which may last longer than three years. Comments from clinical specialists were that ranibizumab had approximately equal effectiveness to bevacizumab but no head to head clinical trials comparing these two treatments against each other are yet available. Neither BRAVO or CRUISE trial compare ranibizumab with dexamethasone implant (current practice).
Section 4 (Consideration of the evidence)	The manufacturer had not compared ranibizumab against bevacizumab as specified in the scope.For CRVO Base case estimates produced by the ERG were an ICER of £43,800 / QALY gained for ranibizumab vsbest supportive care, and £37,400 / QALY vs dexamethasone. The ERG performed an analysis that concludes ranibizumab would need to generate 1.7 times more QALYs than bevacizumab (each month between months 2 and 6) in macular oedema secondary to CRVO to give an ICER at the top end of the range usually considered cost effective. Bevacizumab was dominant over

	ranibizumab in a cost minimization analysis meaning that it is better value for the NHS. Dexamethasone was considered an appropriate comparator as it is currently recommended for use in this indication in the NHS. The Committee said that licensing is not considered a prerequisite for consideration of a comparator in a NICE technology appraisal as long as it is in routine use or is considered best practice. Clinical specialists said that bevacizumab is currently reasonably widely used in the NHS, but the extent of its use varies between centres.
Section 5 (Implementation)	This is a condition for which there have been few treatment options in the past however, recently a number of treatments have become available. These treatments need to be incorporated into a care pathway, with clear selection criteria to ensure cost-effective use of resources. This is difficult when there is limited local experience and no head-to-head evidence comparing the different treatment options.
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	[redacted]
Date	12/15/2011 3:20:00 PM

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	North Yorkshire & York are supportive of the decision on the basis of the evidence presented Health ecomonic evaluation presented
Section 2 (The technology)	We are satisfied that a discount represents the most realistic patient access scheme and hope that any discount will represent a direct discount on the list price meaning any NHS business transactions ane straightforward. Any other scenario (e.g. Paying list price and provider reimbursed a discount as Novartis stock) is not preferred by the commissioner on the basis that this is unnecessarily complex necessitating admin staff to process any discounts in various departments, savings may not be realised.
Section 3 (The manufacturer's submission)	We are disheartened by the lack of manufacturer comparison with bevacizumab, knowing NICE would accept this agent for comparison as license not a prerequisite for a comparator. We would consider bevacizumab is used in clinical practice to varying degrees across the NHS. This organisation is receiving requests for both these anti VEGFs for ophthalmic indications.We note the view of the clinical specialists indicating approximate equal efficacy and in the ERG analysis, bevacizumab would appear to offer more eye health for equivalent investment overall representing better value when resources are scarce. We would wish to clarify admin costs in 3.14, locally admin of Lucentis currently average cost approx £500, this is likely to be similar for other commissioners. Dexamethasone implant should equally be considered as a comparator within the analysis, this is formally now within treatment pathway, realistically as a bridge until NICE determines its position on Lucentis/antiVEGF for RVO. Locally clinicians have proposed there are some patients with glaucoma and retinal haemorrhage in whom laser and dexamethasone are not appropriate, whether cost effective for this group? Uncertain.
Section 4 (Consideration of the evidence)	Consider that the relevant clinical trials have been included noting the lack of evidence for severe ischaemia and outcomes in BRAVO were confounded by rescue laser, and consider a correction to worse seeing eye with corrected utility values appropriate. Whilst accepting the PAS is in commercial confidence, it is difficult to comment on direct costs without detail.
Section 5 (Implementation)	The drug administration schedule and follow up of patients for this service requires significant staffing not only of ophthalmologists to inject but also optometrists and other staff who run the service. Whilst patient numbers are less than DMO or ARMD, it is not clear how much capacity is available within

	the existing infrastructure to extend the service within provider organisations. In terms of the costing template, it is recognised that this can be delivered as an outpatient service. Commissioners would therefore ask that if this is agreed that costs are presented to reflect this.
Section 6 (Proposed recommendations for further research)	Commissioner organisations recognise that NICE did undertake a scoping exercise to evaluate bevacizumab in eye conditions some time ago subject to referral from the Secretary of State to progress with this. It is our belief that the NHS commissioners would wish to see this evaluation undertaken.
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Date	12/14/2011 9:29:00 PM

Name	[redacted]
Role	NHS Professional
Other role	Consultant in Public Health
Location	England
Conflict	yes
Notes	member of TA Committee C. I have not been involved in this appraisal to date. Therefore I am here responding on behalf of the Clinical Commissioning Consortia in Bradford and Airedale
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	we strongly concur wit the Committees preliminary recomendations. This is not a cost effective use of exceptionally scarce resources, there are significant flaws and weaknesses in the manufacturers case. It is entirely inappropriate that the manufacturer did not consider avastin as a comparator (though we understand the commercial reasons for not doing so), but from the perspective of the NHS at local level it is an entirely acceptable comparator. Were the committee to change their preliminary recomendation there would be significnant opportunity cost at local level, with disinvesmtnet in other opthalmology services being seen as necessary should clinicians start to use lucentis in this indication following a positive TA recomendation.
Section 2 (The technology)	without knowing the details of the price agreed with DH, it seems utterly ludicrous to expect the NHS locally to make any detailed plans for the introduction of this technology. Commissioners must know the price of this medicine in this indication and should be a part of the negotiations on price.
Section 3 (The manufacturer's submission)	The manufacturer had not compared ranibizumab against bevacizumab as specified in the scope. A drug currently used in the NHS for this indication, but this was considered by the committee based on analysis done by the ERG. We understand the obvbious commercial reasons for this, given the nature of the corporate chain between Roche, Genentech and Novartis. However, there is consensus and indeed reasonable evidence that VEGFs are superior to steroids, and that there is no compelling evidence that lucentis is any better than avastin (a conclusion also reached by the ERG). It also seems there is reasonable consensus that avastin is an acceptable alternative were lucentis not available to opthalmologists. Therefore we contend strongly that avastin IS a relevant comparator. The clinical trials that assessed the effectiveness of ranibizumab are not fully generalisable to NHS clinical practice! The scope for this technology appraisal included people with or without retinal ischaemia. However both the BRAVO trial, which had assessed RBZ for macular oedema following BRVO and the CRUISE trial which had assessed RBZ for macular oedema following CRVO excluded brisk afferent pupillary defect
Section 4 (Consideration of the evidence)	we concur the the ERGs analysis that avastin is dominant over lucentis, and this should have a strong bearing on the eventual TA recomendation. for BRVO, we agree the manufacturers estimate of £20,500 per QALY gained for ranibizumab versus grid laser photocoagulation seems an underestimation. The ICER for ranibizumab versus dexamethasone for people with BRVO was £31,122.

Section 5 (Implementation)	The NICE costing template TA229 estimates that there are 18 patients with BRVO and 17 patients with CRVO who will be eligible for treatment per 100,000 population. For Bradford and Airedale this equates to approximately 100 patients per year. The costs of lucentis in this indication are not known precisely as there is a confidential PAS and PCTs do not know the price that has been agreed. It is assumed the price will be CONSIDERABLY more expensive than current treatments, thus representing a signficiant incremental net cost for the NHS locally, when considering current treatments. Whislt it is accepted that TA committees are precluded from considering affordability, we would wish to bring to the attention of the committee the not inconsiderable opoortunity cost of sight years forgone as a result of investment in this technology. Commissioners increasingly think in terms of programme budgets, and investment in one area of the eye programme budget must be met by explicit disinvestment elsewhere. There seems to be a reasonable consensus that VEGFs are superior to steroid treatment, and that avastin would be an acceptable alternative.
Section 6 (Proposed recommendations for further research)	Innovativeness of the technology is an important consideration in taking into account considering related technology. In some cases NICE will take into consideration how innovative an intervention is. For ranibizumab the Committee concluded that ranibizumab is one of a group of innovative anti-VEGF treatments, and does not stand alone in this therapeutic area and its benefits are appropriately captured in the QALY calculation.
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Date	12/14/2011 9:49:00 AM

Name	[redacted]
Role	NHS Professional
Other role	
Location	England
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	The clinical trials that assessed the effectiveness of ranibizumab are not fully generalisable to NHS clinical practice The scope for this technology appraisal included people with or without retinal ischaemia. However both the BRAVO trial, which had assessed ranibizumab for macular oedema following BRVO and the CRUISE trial which had assessed ranibizumab for macular oedema following CRVO excluded people with brisk afferent pupillary defect which is severe retinal ischaemia. There is therefore a lack of evidence for the effectiveness of ranibizumab for treatment of RVO in patients with severe ischaemia. Both trials had compared ranibizumab to sham injection rather than treatments used in current clinical practice (bevacizumab and dexamethasone invitreal implants). Although there were differences in the study populations of a study that had assessed dexamethasone (GENEVA), such as time to treatment after emergence of oedema, it was determined that indirect comparisons could be made. Comments from clinical specialists were that ranibizumab had approximately equal effectiveness to bevacizumab but no head to head clinical trials comparing these two treatments against each other
Section 4 (Consideration of the evidence)	Ranibizumab for the treatment of macular oedema secondary to RVO is not a cost effective use of NHS resources The Committee determined that the most plausible ICERs for ranibizumab compared with alternatives were all above the ranges usually considered cost-effective for NHS use (i.e. £20,000 to £30,000 per QALY gained).The manufacturer did not compare its drug against bevacizumab. Bevacizumab (Avastin), like ranibizumab inhibits VEGF. It has marketing authorisation to be used in the treatment of some cancers, but has been used off-license for the treatment of macular oedema at lower doses. Comments from clinical specialists were that ranibizumab had approximately equal effectiveness to bevacizumab but because a license has not been sought for the use of bevacizumab in the eye, its safety in the eye is not assured. Additionally concerns were raised from

	patient experts about the use of unlicensed treatments for which there was no post-marketing surveillance, particularly if there were licensed alternatives. The Committee said that licensing is not considered a prerequisite for consideration of a comparator in a NICE technology appraisal as long as it is in routine use or is c
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Date	12/14/2011 9:44:00 AM

Name	[redacted]
Role	NHS Professional
Other role	Consultant ophthalmologist
Location	England
Conflict	yes
Notes	I received fees from Novartis for work on advisory boards relating to the use of Lucentis.
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	It is deeply disappointing that we do not have access to Lucentis for retinal vein conclusions or diabetic retinopathy. Â The additional time taken by consultants to fill in individual funding requests for all those patients for whom ozurdex is not suitable (glaucoma, ocular hypertension etc) and the cost of the IFR panel sitting has not been costed. There is also the additional time needed in clinic with each patient as we have to explain that the best treatment (safety and efficacy) is Lucentis but they cant have that unless I put in an IFR but they may be able to have ozurdex as an option but our PCT is quibbling about whether an option means it is obliged to pay or not. In addition there is triamcinolone which we have used for years but the manufacturer says we shouldnt use in the eye and then again there is Avastin which NICE reported as being as effective as ozurdex with a better safety profile and probably cheaper but didnt recommend even as an option. There is also a loss of choice here. Some patients may prefer the injection in to their eye to have a small needle(unlike ozurdex) and not to run the risk of cataract and a 25% chance of ending up on glaucoma drops.
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	
Section 4 (Consideration of the evidence)	
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Date	12/10/2011 2:41:00 PM

Name	[redacted]
Role	Public
Other role	
Location	Europe
Conflict	no
Notes	
Comments on individual sections of the ACD:	
Section 1 (Appraisal Committee's preliminary recommendations)	
Section 2 (The technology)	
Section 3 (The manufacturer's submission)	
Section 4 (Consideration of the evidence)	Dear sir/madam A family member has this condition - hence my interest from semi-retirement. While it does seem that this agent is not an appropriate use of NHS resources - the documentation available is perhaps not presented in a manner that can allow accessible feedback Namely - the issuing of an erratum document alongside the main evidence review group means I have found it difficult to work out what is what vis a vis changes/errors etc - SURELY it would be fairer and clearer to issue one finalised AND ACCURATE document - especially as both seem to have been made available for comment at the same time. IS this normal practice? On a more pedantic matter - the erratum document highlights changes made to tables RE sham amended to sham/0.5mg. What does this 0.5 mg mean - I assume volume of sham product injected - if so - this seems too detailed as this would be a natural assumption in such a study Im told. However, I have also been told that it may be that this means sham OR the agent - if so this really should be made clear! I am grateful for this opportunity to comment - a wonderful process Yours sincerely James Brown MA
Section 5 (Implementation)	
Section 6 (Proposed recommendations for further research)	
Section 7 (Related NICE guidance)	
Section 8 (Proposed date of review of guidance)	
Date	11/30/2011 12:06:00 PM