National Institute for Health and Clinical Excellence

**Ranibizumab and pegaptanib for the treatment of age-related macular degeneration**

Royal College of Nursing – Ophthalmic Nursing

## Introduction

With a membership of over 395,000 registered nurses, midwives, health visitors, nursing students, health care assistants and nurse cadets, the Royal College of Nursing (RCN) is the voice of nursing across the UK and the largest professional union of nursing staff in the world. RCN members work in a variety of hospital and community settings in the NHS and the independent sector. The RCN promotes patient and nursing interests on a wide range of issues by working closely with the Government, the UK parliaments and other national and European political institutions, trade unions, professional bodies and voluntary organisations.

The Royal College of Nursing welcomes the opportunity to comment on the Appraisal Consultation Document for the technology appraisal of the use of ranibizumab and pegaptanib for the treatment of age-related macular degeneration.

## RCN Response to the Appraisal Consultation Document

Specialist nurses working in ophthalmology are astounded and deeply concerned by some of the recommendations made by the Appraisal Committee on the appraisal of the use of ranibizumab and pegaptanib for the treatment of age-related macular degeneration.

July 2007

When representatives of the RCN attended the consultees' information meeting for this appraisal, assurance was given by the panel that the appraisal group "had learnt lessons from the past in terms of the PDT findings" and that limiting to 'second eye' would not feature as part of this process, this clearly has not been carried through. We are absolutely convinced that the routine use of AntivegF drugs by retinal specialists to stabilise vision for all patients with wet AMD is fully justified by the evidence base that we have read and which has been put to the Committee. We are amazed to find that important elements of the evidence submitted by all the consultees have been disregarded.

We, therefore, do not support the Appraisal Committee's recommendations that only the most aggressive, fastest progressing type of wet AMD ('predominantly classic') is treated with anti-VEGFs. 'Predominantly classic' type of AMD represents only about 20% of all wet AMD cases - but around half of patients with less aggressive disease (minimally classic or occult) will go on to develop predominantly classic wet AMD within a year, with further vision loss.

Further, AMD is not the only disease process that patients of this age group may experience and imagine the scenario if the 2nd eye - the good eye were to develop say a vein occlusion and the patient had not had the first eye treated as they did not fit the criteria, clearly this has not been given serious thought.

This recommendation is therefore a false economy and risks patients' sight.

We welcome the recommendation that Lucentis is used for AMD but would challenge the stipulation that it be the only option and that Macugen is not recommended for treatment of wet AMD at all. There are differences in action between these two drugs, which may be important in individual cases. Clinicians do not wish to be limited in our treatment options in this way.

With respect to treatment with anti-VEGFs, we are concerned that as in the Photo-Dynamic Therapy appraisal, treatment with anti-VEGFs is only recommended when the patient already has AMD in one eye, and is effectively blind in that eye, and has developed AMD in the second eye. This is completely unacceptable and we are convinced that the Committee would not make such a recommendation were it to be any other part of the anatomy (for instance denying treatment for peripheral vascualr disease

until the patient has lost one leg) - what it means is that people will have to lose significant vision in one eye and then develop symptoms in the other before we attempt treatment which may or may not help - this is absolutely outrageous.

We, therefore, challenge the Appraisal Committee's recommendations and ask that the Committee give serious consideration to the points raised in this response.

**Point 1**

We reiterate that it is unethical and unacceptable to allow someone to go blind in one eye before being eligible for treatment in the second eye. Is the Appraisal Committee suggesting that only one functioning eye is required for normal life? This is patently untrue and there is enough literature available which describes this and the consequences of it. To limit these new treatments to 'second eyes' only, when only one eye is affected would also be setting a disastrous precedent for other ophthalmic treatment areas such as cataract, diabetic retinopathy and glaucoma, vitreo retinal surgery all of which are bilateral in nature!

An ophthalmic clinician's goal is to prevent loss of sight. This is also the aim of all national and international organisations concerned with vision and the notion that avoidable blindness should be allowed and indeed, encouraged is not something one would expect an Appraisal Committee comprising of leading healthcare professionals to recommend!

**Point 2**

The terminology 'no permanent structural damage' to the central fovea is misleading. How can the one judge permanent damage unless one means fibrosis that is long standing? The very fact that the patient has a subfoveal choriodal neovascular membrane (CNV) means there will be some damage in the foveal area. Therefore the Committee's recommendations are excluding the majority of patients with 'Wet AMD'!

Even patients with some central fibrosis at the fovea need treatment to control the disease process and prevent a large central scotoma that would grossly diminish their ability to self care and remain independent.

A study by Wagner (2006) using combined PDT and ranibizumab, demonstrated that in patients with occult CNV, absolute scotoma decreased or remained stable in 83%. Severe relative scotoma also decreased or remained stable in 83% and mild relative scotoma had increased in 50% of patients. Areas of normal macular function improved or stabilized in 83%. In AMD patients this will enhance their ability in relation to visual rehabilitation and possibly preserve their dignity and independence.

**Point 3**

Not recommending the use of antiVegF treatment for minimal classic and occult CNV is to disregard a group of patients for whom currently there is no NHS treatment option and thus they will be forced to seek private health care or loose vision! To exclude these patients regardless of clinical need leaves them with no effective treatment and at high risk of increased dependence and injury. Therefore we can only reasonably infer that the Committee has not taken account of the available evidence of clinical need and national health priorities, focusing only on financial aspects of these therapies.

**Point 4**

Limiting treatment to only the predominantly classic subgroup of patients is unacceptable, particularly when there are good results with occult and mixed - so only patients with classic disease have a possibility of remission, adding to the moral dilemma and burden of NHS workers. Already we have to inform our patients that their wet AMD is treatable and there is a good chance that we can prevent further sight loss but unfortunately because they do not have a predominantly classic lesion we cannot provide their treatment on the NHS! This causes distress to both parties and has an added burden on clinic time as these patients need time and empathy not only to accept their diagnosis but understanding why there is no treatment available to them! In addition the costs to the individual, the family and the community are massive. We know from the vast evidence produced by the Royal National Institute for the Blind and the Macular Disease Society and from clinical practice that visual impairment leads to loss of employment, dependency on state benefits, restricted mobility, family break-up and social exclusion. Surely the benefits of preventing blindness vastly outweigh the costs of treatment.

July 2007

**Point 5**

The number of treatments used in the manufacturer's model is the number indicated in the licence indication for Ranibizumab based on the scientific findings of the PRONTO study. In this study, following initial 3 injections over the first three months, re-treatment with Ranibizumab was performed only if there was an increase in central OCT thickness of at least 100 µm, a loss of 5 letters in conjunction with recurrent fluid by OCT, new onset classic neovascularisation, or new macular haemorrhage. We feel that based on this protocol, the number of treatments quoted in the model is a realistic guide on which to map costs to the NHS.

As clinicians we are very aware that few interventions continue to be used in routine practice in precisely the same way as that reported in RCTs. However, this is more because RCTs are by their very nature insufficiently flexible to allow for individualisation of treatment than because the treatment regimens evaluated in RCTs need to be entirely reconsidered.

The optimal treatment is likely to be patient dependent and appropriate treatment regimens for the individual patient can only be properly determined in routine clinical use. It is true that we do not know what the optimal regimen is at this point in time, but the right thing to do is to implement as close to the trial protocol as possible and then set up studies to answer questions on dosage regimen and also the effects of substituting Lucentis with other agents in a graded manner.

This can be monitored under the clinical governance agenda of the providers. All routine practice is presently monitored through clinical audit and quality assurance outcome measures. The Committee can be reassured that in the current climate all clinicians are painfully aware of their accountabilities to the NHS as well as their patients and therefore will make the best evidence-based cost effective clinical decisions for all concerned.

**Point 6**

We note that the Committee has estimated the cost of these new treatments as a day case rather than an out patient procedure.

Cost should not be the driving factor but quality of life and the long term anxiety expressed by patients who have AMD in a first eye. Well documented findings have shown that patients have spent many hours worrying about how they will cope if their second eye develops the disease causing them anxiety and depression.

The introduction of anti-VegF intravitreal treatments will mean a considerable increase in workload. In addition many units will need to provide additional services i.e. 'fast track' clinics, and because patients will potentially need monthly visits, staff numbers will need to increase to sustain demand. Therefore, despite the fact that the assessment and injection procedure takes no longer than that of photodynamic therapy (PDT), centres will need this additional funding as cost for day cases to develop services. The cost should be balanced against the fact that, over time as clinical experience and knowledge re- use of these treatments grows, the number of treatments will be less as seen with PDT, and therefore cost to the NHS will decrease.

There appears to be no evidence in the document that the appraisal has looked at costs in terms of the family unit. Many of the patients that present at clinics are aged between 60 - 75 and these patients can be carers of grand children, spouse and also carers of elderly relatives thus by denying treatment to this one person could have a huge impact on all areas of family network!

Further, costs related to blindness, including low-vision aids, visual rehabilitation and community care should be taken into account - these are added costs (to the state). The Committee also does not appear to have taken account of the losses incurred by the patient in terms of their salary or their spouse's, who has to care for them or both.

**Point 7**

The Committee suggests that cost effectiveness is sensitive to uptake. We would suggest that there will be a very high uptake in these new treatments in the NHS, therefore costs will be lower and outcomes for wet AMD patients better. Already some eye units have seen an increase in referrals and enquiries as to whether or not they can offer treatment. Patients, relatives and carers are prepared to spend money travelling to clinics at frequent intervals and to remain under observation for years if we can save

even a small amount of their sight. If this is the case surely we should not deny them the opportunity.

Monthly treatments could also be restrictive for many patients and make it impossible for them to agree to commence on this therapy, a 6 weekly treatment could be an option that would be easier to comply with. In the current guidance this option has been discounted completely as macugen has not been recommended for any lesion type.

**Point 8**

We find it difficult to understand how the Committee of an organisation whose remit is to examine evidence and recommend best practice, is recommending a head to head trial with a drug that is not licensed for use in the eye!

Further, it is interesting to note that both drugs have been approved for use in Scotland, in all circumstances (i.e. not just the one eye and not for just occult) and they have obviously done similar appraisal work, yet this is refused in England and Wales. It would be ill-advised for such inequalities to exist across the countries, particularly as the appraisal was based on similar evidence and the patients are governed by the same National Health Service principles.

We welcome the recommendation for an investigation into the long term effects and optimal regimen of antivegF treatments but strongly recommend that this be done via a national audit not as with PDT a 'study' that diverted necessary funding away from the clinical area.

**Summary**

We acknowledge that the Appraisal Committee has a very difficult job reviewing numerous new therapies available to the NHS but ask the Committee to re-examine the evidence for antiVegF treatments for all wet AMD in the light of this response. We strongly believe, as do other health professional colleagues that the evidence justifies the routine use of antiVegF treatments by retinal specialists to stabilise vision for all patients suffering the debilitating effects of wet AMD. We are already seeing dramatic results in clinical practice. Our patients are not only getting stability but improvement in

vision when VegFs are used. We owe it to these vulnerable elderly patients to allow them the dignity to remain as independent as possible by providing these treatments on the NHS.

We would recommend that macugen stays as an option as it has a different effect.

## Reference

Wagner J, et al (2006) changes in functional mapping in patients with neovascular Age-related macular degeneration receiving combination of verteporfin and Randibizumab therapy Invest Ophthalmol Vis Sci 2006; 47: E-Abstract 363