NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

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

Final scope

Appraisal objective

To appraise the clinical and cost effectiveness of ranibizumab and pegaptanib within their licensed indications for age-related macular degeneration, and to provide guidance to the NHS in England and Wales[1].

Background

The macula is the central part of the retina responsible for colour vision and perception of fine detail. Age-related macular degeneration (ARMD) is one of the leading causes of irreversible sight loss in people over the age of 50 years. ARMD is associated with loss of central vision with opaque or dark patches and distortion of vision. There are two main types of ARMD, wet (neovascular) and dry (non-neovascular) ARMD. Dry ARMD progresses more slowly than wet ARMD, causing a less dramatic loss of retinal pigment cells and photoreceptor cells. Wet ARMD is characterised by the formation of immature blood vessels that grow between the retinal pigment epithelial cells and the photoreceptor cells in the centre of the retina. This is known as choroidal neovascularisation (CNV). These blood vessels easily haemorrhage and cause scarring in the macula leading to vision impairment. Wet ARMD usually progresses much more quickly than dry ARMD. There are approximately 26,000 new cases of wet ARMD in the UK each year.

CNV can be sub-classified into the classic (classic no occult, predominantly classic and minimally classic) and the occult form according to its appearance on investigation by fluorescein angiography, and according to the location of the lesion in relation to the fovea, which is a small depression in the macula that provides the clearest vision: subfoveal (extending behind the middle of the fovea); juxtafoveal (in the remainder of the fovea but not the middle) and extrafoveal (in the macula excluding the fovea).

People with macular degeneration retain their peripheral vision but lose central vision. Loss of central vision, particularly when affecting both eyes, is associated with a loss of quality of life, affecting the ability to read, recognise faces and drive, and with an increased risk of falls and potentially significant loss of independence. Rapidly deteriorating vision has a major impact on emotional wellbeing and individuals are likely to suffer depression and anxiety.

[1] The Department of Health remit: "to appraise the clinical and cost effectiveness of anecortave acetate, ranibizumab and pegaptanib in their licensed indications for age-related macular degeneration". After the referral of the remit to NICE, the application for marketing authorisation for anecortave acetate was withdrawn by the manufacturer.

For most patients with ARMD, management consists of 'best supportive care'. Visual rehabilitation, with teaching of skills and the provision of equipment to facilitate reading and other activities of daily living, may help people make the most of their remaining vision. The aim of therapy for people with wet ARMD is to alter the progression of vision loss.

Currently, photocoagulation and photodynamic therapy (PDT) are the main interventions used to arrest the proliferation of blood vessels in wet ARMD. Photocoagulation is used for extrafoveal CNV, and this only accounts for a small proportion of cases. The drugs under appraisal have not been evaluated in people with extrafoveal CNV. PDT aims to destroy CNV lesions without damaging the overlying retina, so it can be used for subfoveal lesions. The treatment involves the infusion of a light-sensitive drug, followed by light activation of the drug. At present only verteporfin is licensed for this indication, but other agents are in development. Current NICE guidance recommends the use of verteporfin only for individuals who have a confirmed diagnosis of classic with no occult subfoveal wet ARMD. The use of PDT in occult CNV associated with wet ARMD was not considered because verteporfin was not licensed for this indication when the appraisal began.

The technologies

Both drugs covered in this appraisal act as anti-angiogenic agents, that is they inhibit the further growth of neovascular membranes and therefore prevent further development of the condition. Clinical studies for both drugs have been carried out in people with subfoveal CNV.

Ranibizumab (Lucentis, Genentech/Novartis Pharmaceuticals UK Ltd) is an anti-vascular endothelial growth factor (VEGF) antibody fragment. It is administered as monthly intravitrial injections (into the eyeball) at a dose of 0.3-0.5 mg for as long as the patient benefits. A UK licence for the improvement and maintenance of visual acuity and function, and for the reduction of vascular leakage and retinal oedema, in patients with wet ARMD, is expected at the end of 2006.

Pegaptanib sodium (Macugen, Pfizer Ltd) is a selective VEGF inhibitor. Pegaptanib binds to extracellular VEGF thereby preventing VEGF from binding to its receptor. It is administered as an intravitrial injection at a dose of 0.3 mg every 6 weeks for as long as the patient benefits. Pegaptanib is licensed in the UK for the treatment of wet ARMD.

Interventions	Ranibizumab and pegaptanib within their licensed indications
Populations	People with the subfoveal CNV associated with wet ARMD

Standard comparators	Best supportive care In addition, for the subgroup of individuals with a confirmed diagnosis of classic with no occult subfoveal wet ARMD, PDT with verteporfin is also a comparator.
Outcomes	Outcomes should include: • Visual acuity • Contrast sensitivity • Adverse effects of treatment • Adherence to treatment • Health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The economic evaluation should be based on an appropriate time horizon over which the main costs and benefits of treatment are likely to differ from the standard comparator. If trial evidence does not allow a comparison to the current standard comparator, indirect comparison should be considered. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	If appropriate, consideration will be given to subgroups for whom the technologies are particularly appropriate. Potential subgroups could be defined according to the location of the lesion, and the composition of the lesion in terms of classic and occult CNV. Where the licensed indication and the evidence allows combination of the drugs with photodynamic therapy should be considered.

Related NICE recommendations	Related technology appraisals: NICE Appraisal Guidance No.68 – The use of photodynamic therapy for the treatment of age related macular degeneration (September 2003). Related guidelines: NICE Interventional Procedure Guidance No. 48 – Macular translocation for age-related macular degeneration (March 2004) NICE Interventional Procedure Guidance No. 49 – Radiotherapy for age-related macular degeneration (March 2004) NICE Interventional Procedure Guidance No. 58 – Transpupilary thermotherapy for age-related macular degeneration (June 2004)