

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Anecortave acetate, ranibizumab and pegaptanib for the treatment of age-related macular degeneration

Draft scope

Draft remit/appraisal objective

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

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 a gradual painless 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 is more benign and associated with a discrete loss of retinal pigment cells. Wet ARMD is characterised by the formation of abnormal 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 16,000 new cases of wet ARMD in the UK each year.

CNV can be sub-classified into the classic form and occult form according to its appearance on investigation by fluorescein angiography. In classic CNV the blood vessels can be seen distinctively, whereas in occult CNV the vessels are difficult to locate. Classic and occult CNV can occur within the same lesion. CNV can be further sub-classified depending on 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).

When both eyes are affected, loss of central vision is associated with a dramatic loss of quality of life, affecting the ability to read, recognise faces and drive. People with macular degeneration retain peripheral vision so they do not become completely blind. However their vision may become very poor, with complete or near-complete loss of central vision leading to significant loss of independence. Rapidly deteriorating vision has a major impact on emotional wellbeing and individuals are likely to suffer depression and anxiety.

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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 there are two main interventions that attempt to arrest the proliferation of blood vessels in wet ARMD:

- Photocoagulation is used for extrafoveal CNV, and this only accounts for around 10-15% of cases. A laser is used to burn away the neovascular membranes and halt the rapid vision loss associated with their progression, which results in a dark scotoma and a visual field defect. For this reason it is not used for lesions affecting the centre of the field of vision.
- Photodynamic therapy (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

All three drugs covered in this appraisal act through an anti-angiogenic approach, that is they inhibit the formation of neovascular membranes and therefore prevent further development of the condition.

Anecortave acetate (Retaane, Alcon Inc) is an analogue of hydrocortisone acetate. It is administered as a juxtasclear depot suspension delivered via a cannula in conjunction with a counter pressure device to control reflux at a dose of 15mg every six months for as long as the patient benefits. A UK license for the treatment of wet ARMD is expected within the timeframe of this appraisal.

Ranibizumab (Lucentis, Genentech/Novartis) is an anti-vascular endothelial growth factor (VEGF) antibody. It is administered as monthly intravitreal injections at a dose of 0.3-0.5mg for as long as the patient benefits. A UK license 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) is a selective VEGF inhibitor. Pegaptanib is a pegylated modified oligonucleotide aptamer and its three dimensional structure allows it to bind to extracellular VEGF. This results in selective inhibition of VEGF binding to its receptor. It is administered as an

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intravitreal injection (into the eyeball) at a dose of 0.3mg every 6 weeks for as long as the patient benefits. Pegaptanib is licensed in the UK for the treatment of wet ARMD.

Interventions	Anecortave acetate, ranibizumab and pegaptanib within their licensed indications
Populations	People with wet ARMD
Standard comparators	Best supportive care For the subgroup of individuals with a confirmed diagnosis of classic with no occult subfoveal wet ARMD, PDT with verteporfin is also a comparator. For extrafoveal lesions, photocoagulation is a comparator.
Outcomes	Outcomes should include: <ul style="list-style-type: none"> • Visual acuity • Contrast sensitivity • Number of treatments • Adverse effects of 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.

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

- Are the comparators sufficiently clearly defined?
- Can the population (classic, occult, subfoveal, extrafoveal CNV) be sufficiently defined as the licensed indications are not yet known for two of the drugs?
- Will the new drugs be used instead of PDT and/or photocoagulation, or possibly in combination with PDT (as undertaken in one study)?
- What is the intensity and duration of treatment?