NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Ranibizumab for the treatment of macular oedema caused by retinal vein occlusion (RVO)

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ranibizumab within its licensed indication for the treatment of macular oedema caused by retinal vein occlusion (RVO).

Background

The macula is the central part of the retina responsible for colour vision and perception of fine detail. Macular oedema refers to the accumulation of fluid within the retina at the macular area, which can lead to severe visual impairment in the affected eye.

RVO is a common cause of reduced vision due to retinal vascular disease. It is classified into central retinal vein occlusion (CRVO) and branch retinal vein occlusion (BRVO). CRVO results from thrombosis of the central retinal vein where it passes through the back of the optic nerve through a mesh-like structure called the lamina cribrosa. BRVO is caused by venous thrombosis at an arteriovenous crossing, where an artery and vein share a common lining of connective tissue.

Thrombosis of the retinal veins causes an increase in retinal capillary pressure resulting in increased capillary permeability and the discharge of blood and plasma into the retina. This leads to the development of macular oedema and varying levels of ischaemia through non-perfusion of capillaries. These changes trigger an increased amount of vascular endothelial growth factor (VEGF), which increases vascular permeability and new vessel proliferation.

No prevalence or incidence data has been identified for England and Wales. However a recent US study reported a 15 year incidence of 500 new cases per 100,000 population for CRVO and 1800 cases per 100,000 population for BRVO. The Royal College of Ophthalmologists 2010 interim guidelines for the management of RVO suggest that around half of these cases would require treatment for visual impairment. Incidence increases with age. Other risk factors include hypertension, hyperlipidaemia, glaucoma, thrombophilia and diabetes.

Both BRVO and CRVO can be broadly divided into two sub-categories: ischaemic and non-ischaemic, the former being the more severe. Non-ischaemic CRVO may resolve completely without any complications or may

progress to the ischaemic type. In more than 90% of patients with ischaemic CRVO, final visual acuity may be 6/60 or worse. BRVO presents with a variable degree of visual loss; approximately 50-60% of untreated eyes with BRVO retain a visual acuity of 6/12 or better after one year, whilst 25% will have a vision of less than 6/60. The impact of vision loss associated with RVO can have a profound effect on vision-related quality of life. Patients may struggle with daily tasks, lose confidence and become increasingly dependent on family and carers. RVO is also associated with an increase in vascular causes of death.

Current treatment options aim to preserve vision and prevent complications. Dexamethasone implant has a UK marketing authorisation for macular oedema following either BRVO or CRVO. For BRVO, a grid pattern of photocoagulation may be beneficial where visual loss is not severe. Other medical interventions currently used in clinical practice include intravitreal injections of bevacizumab and occasionally intravitreal injections of triamcinolone (IVTA); both are not licensed for the treatment of macular oedema secondary to RVO and the triamcinolone formulation available in the UK (Kenalog) is contraindicated for ocular use. Laser anastomosis and optic nerve sheathotomy are surgical procedures which have been studied in clinical trials but these are rarely undertaken in current clinical practice in the UK.

The technology

Ranibizumab (Lucentis, Novartis Pharmaceuticals) is a humanised therapeutic antibody fragment that binds to VEGF-A isoforms of VEGF thereby preventing binding of VEGF-A to receptors VEGFR-1 and VEGFR-2. It is administered through intravitreal injection.

Ranibizumab does not currently hold a UK marketing authorisation for the treatment of macular oedema with RVO. It is being studied in clinical trials in people with visual impairment due to macular oedema secondary to central retinal vein occlusion compared with sham injection and in trials in people with visual impairment due to macular oedema secondary to branch retinal vein occlusion compared with sham injection.

Intervention(s)	Ranibizumab
Population(s)	People with visual impairment due to macular oedema caused by retinal vein occlusion (RVO)

Comparators	CRVO: i. Best supportive care (ischaemic only) ii. Bevacizumab iii. Dexamethasone implant BRVO: i. Best supportive care (ischaemic only) ii. Bevacizumab iii. Dexamethasone implant iv. Grid pattern photocoagulation
Outcomes	The outcome measures to be considered include: • Visual acuity (the affected eye) • Visual acuity (the whole person) • 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 reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.

Other considerations	If the evidence allows, consideration will be given to subgroups according to: • type of RVO (BRVO and CRVO) • the presence or absence of ischaemia • baseline visual acuity • baseline structural damage to the central fovea • perfusion at the back of the eye • duration of macular oedema (time since diagnosis). Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 155, Aug 2008, 'Ranibizumab and pegaptanib for the treatment of age-related macular degeneration'. Review date August 2011. Technology Appraisal No. 68, Sep 2003, 'Guidance on the use of photodynamic therapy for age-related macular degeneration'. Technology Appraisal in Preparation, 'Ranibizumab for the treatment of diabetic macular oedema'. Earliest date of publication TBC. Technology Appraisal in Preparation, 'Dexamethasone intravitreal implant for the treatment macular oedema caused by retinal vein occlusion'. Earliest date of publication June 2011. Technology Appraisal in Preparation, 'Fluocinolone acetonide intravitreal insert for the treatment of diabetic macular oedema'. Earliest date of publication TBC. Proposed Technology Appraisal, 'Pegaptanib sodium for the treatment of diabetic macular oedema'. Related Interventional Procedures: Interventional Procedure No. 72, Jul 2004, 'Arteriovenous crossing sheathotomy for branch retinal vein occlusion'. Interventional Procedure No. 48, Mar 2004, 'Macular translocation for age-related macular degeneration'. Interventional Procedure No. 49, Mar 2004, 'Radiotherapy for age-related macular degeneration'.

	Interventional Procedure No. 58, Jun 2004, 'Transpupillary thermotherapy for age-related macular degeneration'. Interventional Procedure No. 272, Aug 2008, 'Implantation of miniature lens systems for advanced age-related macular degeneration'.