NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Technology Appraisal

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

Draft scope (Pre-referral)

Draft remit/appraisal objective

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

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.

Retinal vein occlusion is a common vascular disorder of the retina and can lead to severe visual loss. Central retinal vein occlusion (CRVO) is a type of retinal vein occlusion that 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.

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. Incidence increases with age. Other risk factors include hypertension, hyperlipidaemia, glaucoma, thrombophilia and diabetes.

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.

Patients with CRVO can become dependent, struggle with daily tasks and have a loss of confidence. Retinal vein occlusions are also associated with an increase in vascular causes of death.

There is no early treatment that will alter the visual prognosis in established CRVO. The aims of current treatments are to preserve vision and prevent complications. Medical interventions currently used in clinical practice include intravitreal injections of triamcinolone (IVTA) and intravitreal injections of bevacizumab; both are not licensed for the treatment of macular oedema secondary to CRVO. Laser photocoagulation is a surgical alternative.

The technology

Ranibizumab (Lucentis, Novartis) 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 CRVO. It is being studied in clinical trials in people with macular oedema secondary to central retinal vein occlusion compared with sham injection.

Intervention(s)	Ranibizumab
Population(s)	People with macular oedema caused by central retinal vein occlusion (CRVO)
Comparators	• Triamcinolone acetonide (IVTA) • Bevacizumab • Dexamethasone (subject to licence)
Outcomes	The outcome measures to be considered include: • Visual acuity (the affected eye) • Visual acuity (the whole person) • Contrast sensitivity • 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: • the presence or absence of ischaemia; • baseline visual acuity; • baseline structural damage to the central fovea. 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'. 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'.

Questions for consultation

Have the most appropriate comparators for ranibizumab been included in the scope?

- Is surgery a relevant comparator? If so, which surgical techniques are currently used in clinical practice?
- Are the other comparators listed routinely used in clinical practice?

Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of patients in whom the technology is expected to be

more clinically effective and cost effective or other groups that should be examined separately?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)