NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Ranibizumab for the treatment of diabetic macular oedema

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ranibizumab within its licensed indication for the treatment of diabetic macular oedema.

Background

The macula is the central part of the retina responsible for colour vision and perception of fine detail. Diabetic macular oedema (DMO) is the main cause of visual loss in diabetic maculopathy, a type of diabetic eye disease which involves localised damage to the macula. DMO occurs as a result of changes in retinal blood vessels in people with diabetes. A reduction in the number of connective tissues around capillaries and an increased amount of vascular endothelial growth factor (VEGF) causes increased permeability of the blood-retinal barrier. This leads to leakage of plasma constituents in the surrounding retina, causing oedema which disrupts the fovea, the area responsible for sharp vision. It can lead to severe visual impairment in the affected eye.

Diabetic maculopathy can be classified as focal, diffuse, ischaemic or mixed, depending on the location of leakage or loss of blood supply due to capillary loss. Focal maculopathy is caused by localised leakage of tissue fluid from tiny swellings in the wall of retinal capillaries. Diffuse maculopathy is caused by widespread leakage from dilated capillaries leading to generalised thickening of the central macula. Ischaemic maculopathy is caused by the blood vessels in the macula becoming constricted; this starves the macula of oxygen and nutrition, and is associated with a significant risk to vision. Mixed maculopathy refers to cases with a combined pathology, particularly of diffuse oedema and ischaemia.

The majority of visual loss occurs when DMO involves the centre of the macula. This is known as clinically significant macular oedema (CSMO) and is regarded as the threshold for treatment. CSMO occurs if there is thickening of the retina involving the centre of the macula and if there are hard exudates.

In 2009 the number of people diagnosed with diabetes in England and Wales was 2.4 million. Approximately 14% of people with diabetes have DMO and prevalence increases to 29% for people with diabetes who use insulin for more than 20 years. When DMO is untreated there is a 25-30% risk of developing CSMO. Moderate visual loss will occur in approximately 24% of untreated eyes after 2 years where CSMO has developed. There are no established prevalence rates of centre-involving DMO in England and Wales. In addition to duration of diabetes, risk factors include older age, poor glucose control, high blood pressure, nephropathy (kidney disease), pregnancy,

smoking, obesity and having a high cholesterol level. Diabetes is more common in African-Caribbean and South Asian people.

Treatment of systemic risk factors, including dietary modification and blood pressure control, may delay disease progression. The main treatment option for sight-threatening focal, diffuse or mixed DMO is laser therapy (photocoagulation). The aim of photocoagulation is to prevent further visual loss. Visual loss with ischaemic maculopathy cannot be treated. There are currently no licensed pharmacological agents to treat DMO. In some clinical centres in the NHS, bevacizumab is used outside its licensed indication where photocoagulation has failed to produce a response or as an alternative treatment option where long term treatment with photocoagulation is considered a risk.

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 have a UK marketing authorisation for the treatment of DMO. It has been studied in clinical trials of people with visual impairment due to centre-involving DMO as a monotherapy compared to sham injection and photocoagulation. It has also been studied as a combination therapy with photocoagulation compared to triamcinolone with photocoagulation and photocoagulation monotherapy.

Intervention(s)	Ranibizumab monotherapy Ranibizumab in combination with laser photocoagulation
Population(s)	People with visual impairment due to diabetic macular oedema
Comparators	• Laser photocoagulation • Bevacizumab • Ranibizumab monotherapy and ranibizumab in combination with laser photocoagulation will be compared with each other
Outcomes	The outcome measures to be considered include: • Best corrected visual acuity (the affected eye) • Best corrected visual acuity (both eyes) • 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: • type of DMO (focal, diffuse or mixed); • baseline visual acuity; Guidance will only be issued in accordance with the marketing authorisation. If evidence allows consideration be given to the possible advantage that the aim of treatment with ranibizumab is to improve vision bearing in mind that the aim of current treatments is to prevent further loss of vision.
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 Aug 2011. Technology Appraisal No. 68, Sep 2003, 'Guidance on the use of photodynamic therapy for age-related macular degeneration'. Review date August 2011. Technology Appraisal in Preparation, 'Ranibizumab for the treatment of macular oedema caused by central retinal vein occlusion'. Earliest date of publication TBC. Technology Appraisal in Preparation, 'Dexamethasone for the treatment of macular oedema caused by retinal vein occlusion'. Earliest date of publication TBC. Proposed Technology Appraisal, 'Fluocinolone acetonide intravitreal insert for the treatment of diabetic macular oedema'. 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'. Related Guidelines: Clinical Guideline No.15, Jul 2004, 'Type 1 diabetes: diabetes and management of type 1 diabetes in children, young people and adults'. Review date Jan 2013. Clinical Guideline No.66, May 2008, 'Type 2 diabetes: the management of type 2 diabetes'. Review date May 2011.