NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Aflibercept for treating diabetic macular oedema

Final scope

Final remit/appraisal objective

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

Background

Diabetic macular oedema (DMO) is a common complication associated with diabetic retinopathy, and is the most common cause of visual impairment in diabetes mellitus. It occurs as a result of changes in retinal blood vessels in people with diabetes. Disruption of the blood–retinal barrier allows fluid to leak from blood vessels in the central part of the retina (the macula), leading to fluid accumulation and thickening of the macula. This can lead to severe visual impairment in the affected eye.

DMO can be classed as focal diffuse or ischaemic (although no universal definition has been agreed). The majority of vision 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.

There were approximately 2.7 million people aged 17 and over diagnosed with diabetes in England in 2013. Diabetes is more common in people of African–Caribbean and South Asian family origin than in those of European family origin. Approximately 7% of people with diabetes have DMO, of whom 39% have CSMO. The prevalence of DMO is related to the duration and severity of diabetes, and to numerous risk factors including age, pregnancy, smoking, hypertension, nephropathy, obesity and high cholesterol.

Good management of diabetes and other risk factors may delay the onset and progression of DMO, and may involve diet and lifestyle modification, blood pressure control and pharmacological treatments. For DMO specifically, the main treatment options include laser photocoagulation and ranibizumab. NICE technology appraisal TA274 recommends ranibizumab as an option for treating visual impairment due to DMO if the eye has a central retinal thickness of 400 micrometres or more at the start of treatment. NICE technology appraisal TA301 recommends fluocinolone acetonide intravitreal implants as an option for treating chronic DMO that is insufficiently responsive to available therapies if the implant is to be used in an eye with an intraocular (pseudophakic) lens. In addition, bevacizumab is used outside its marketing authorisation in some NHS centres in people for whom ranibizumab is not appropriate.

The technology

Aflibercept solution for injection (Eylea, Bayer Pharma) is a soluble vascular endothelial growth factor (VEGF) receptor fusion protein which binds to all forms of VEGF-A, VEGF-B, and the placental growth factor. Aflibercept is administered by intravitreous injection.

Aflibercept does not currently hold a UK marketing authorisation for treating DMO. The Committee for Human Medicinal Products (CHMP) of the European Medicines Agency (EMA) has issued a positive opinion in June 2014 to grant a marketing authorisation with a therapeutic indication for the treatment of adults with visual impairment due to DMO. It is being studied in clinical trials compared with laser photocoagulation, bevacizumab and ranibizumab in adults with DMO.

Aflibercept solution for injection has a UK marketing authorisation for other conditions, that is, the treatment of neovascular (wet) age-related macular degeneration (AMD), and macular oedema secondary to central retinal vein occlusion (CRVO).

Intervention(s)	Aflibercept
Population(s)	People with visual impairment because of diabetic macular oedema
Comparators	• Laser photocoagulation alone The following technologies alone or in combination with laser photocoagulation: • Ranibizumab • Corticosteroids (including fluocinolone acetonide intravitreal implant and dexamethasone) • Bevacizumab (for people in whom ranibizumab and fluocinolone acetonide intravitreal implants are unsuitable)

Outcomes	The outcome measures to be considered include: • Best corrected visual acuity (affected eye) • Best corrected visual acuity (both eyes) • Central foveal subfield thickness • Contrast sensitivity • Mortality • Need for cataract surgery • Adverse effects of treatment, including cataract formation and glaucoma • Health-related quality of life, including the effects of changes in visual acuity.
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. The availability of any patient access schemes for the intervention or comparator technologies should be taken into account. The cost effectiveness analysis should include consideration of the benefit in the best and worst seeing eye.

Other considerations	If evidence allows, consideration will be given to subgroups according to: • baseline visual acuity • baseline central retinal thickness • treatment history (including people who have received no prior treatment, and those who have received and/or whose disease is refractory to laser photocoagulation, ranibizumab or bevacizumab) • prior cataract surgery (presence of pseudophakic lens). Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Technology Appraisal 301, Nov 2013, 'Fluocinolone acetonide intravitreal implant for the treatment of chronic diabetic macular oedema after an inadequate response to prior therapy'. Review proposal date Nov 2016. Technology Appraisal No. 274, Feb 2013, 'Ranibizumab for treating diabetic macular oedema (rapid review of technology appraisal guidance 237)'. Review proposal date February 2015. Suspended Technology Appraisal 'Pegaptanib sodium for the treatment of diabetic macular oedema'. Related Guidelines: Clinical Guideline in Preparation No. 87, May 2009, 'Type 2 diabetes: the management of type 2 diabetes' (partial update of CG66). Update in progress. Earliest anticipated date of publication Aug 2015. Clinical Guideline in Preparation No. 66, May 2008, 'Type 2 diabetes: the management of type 2 diabetes' (partially updated by CG87). Update in progress. Earliest anticipated date of publication Aug 2015. Clinical Guideline in Preparation No. 15, Jul 2004, 'Type 1 diabetes: diabetes and management of type 1 diabetes in children, young people and adults'. Update in progress. Earliest anticipated date of publication Aug 2015.

	Related Quality Standards: Quality Standard No. 6, Mar 2011, 'Diabetes in adults quality standard'.
Related National Policy	NHS England Prescribed Specialised Services: 13. Adult specialist ophthalmology services http://www.england.nhs.uk/wp-content/uploads/2012/12/pss-manual.pdf National Service Framework: Diabetes, Dec 2001. https://www.gov.uk/government/publications/national-service-framework-diabetes