NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Aflibercept solution for injection for treating diabetic macular oedema

Draft scope (pre-referral)

Draft 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. When DMO is left untreated, there is a 25–30% risk of developing CSMO.

More than 2.6 million people have been diagnosed with diabetes in England and Wales (2011), and this condition 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. It is being studied in clinical trials compared with laser photocoagulation, bevacizumab and ranibizumab in in adults with DMO. Aflibercept solution for injection has a UK marketing authorisation for adults for 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 diabetic macular oedema
Comparators	• Laser photocoagulation alone The following technologies alone or in combination with laser photocoagulation: • Ranibizumab • Fluocinolone acetonide intravitreal implant • Bevacizumab
Outcomes	The outcome measures to be considered include: • Best corrected visual acuity (the affected eye) • Best corrected visual acuity (both eyes) • Contrast sensitivity • Mortality • 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. The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.
Other considerations	If evidence allows, consideration will be given to subgroups according to: • type of DMO (focal or diffuse, central involvement, ischaemic or non-ischaemic maculopathy) • baseline visual acuity • baseline central retinal thickness • previous 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 Guidance will only be issued in accordance with the marketing authorisation.
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 No. 87, May 2009, 'Type 2 diabetes:

	the management of type 2 diabetes' (partial update of CG66). Update in progress (publication date TBC). Clinical Guideline No. 66, May 2008, 'Type 2 diabetes: the management of type 2 diabetes' (partially updated by CG87). Update in progress (publication date TBC). Clinical Guideline No. 15, Jul 2004, 'Type 1 diabetes: diabetes and management of type 1 diabetes in children, young people and adults'. Update in progress (publication date TBC). 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

Questions for consultation

Have all relevant comparators for aflibercept been included in the scope? Which treatments are considered to be established clinical practice in the NHS for DMO?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which aflibercept will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by

making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

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)