NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Aflibercept solution for injection for the treatment of macular oedema caused by central retinal vein occlusion

Draft scope

Draft remit/appraisal objective

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

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 (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.

Thrombosis of the retinal veins increases retinal capillary pressure leading to increased capillary permeability and the discharge of blood and plasma into the macula. These changes trigger an increased amount of vascular endothelial growth factor (VEGF), which increases vascular permeability and mediates new vessel proliferation.

RVO affects 1–2% of people aged over 40 years. Macular oedema, which is the most frequent cause of vision loss in people with RVO, occurs in 84% of all CRVO cases. In England and Wales, it has been estimated that for every 100,000 population, approximately 17 people aged 40 years or over will require treatment for macular oedema following CRVO annually. CRVO typically increases with age, with over 90% of people with CRVO aged above 50 years. It occurs slightly more frequently in males than females and shows no racial preference.

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. 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 CRVO or BRVO. Other medical interventions include anti-VEGF agents such as intravitreal injections of bevacizumab, which is not licensed for the treatment of any ocular condition, and ranibizumab, which is currently undergoing appraisal by the National Institute for Health and Clinical Excellence. There is currently no established treatment for ischemic macular oedema secondary to CRVO in the UK.

The technology

Aflibercept (brand name unknown, Bayer) is a fully human, soluble VEGF receptor fusion protein that binds to VEGF factor-A and Placental Growth Factor and may prevent the inappropriate growth of new blood vessels in the retina, decrease vascular permeability, and reduce oedema. Aflibercept is administered via intravitreal injection.

Aflibercept solution for injection does not currently have a UK marketing authorisation for the treatment of macular oedema caused by CRVO. It has been studied in clinical trials as first-line treatment in adults with centre-involved macular oedema secondary to CRVO compared with sham intravitreal injections.

Intervention(s)	Aflibercept solution for injection
Population(s)	Adults with visual impairment due to macular oedema caused by central retinal vein occlusion.
Comparators	• dexamethasone implant • bevacizumab • ranibizumab (subject to on-going NICE appraisal) • best supportive care (including laser anastomosis for ischaemic CRVO only)
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: • 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. 229, Jul 2011, 'Dexamethasone intravitreal implant for the treatment of macular oedema caused by retinal vein occlusion'. Review date Jan 2014. Technology Appraisal in Preparation, 'Ranibizumab for the treatment of macular oedema caused by retinal vein occlusion'. Earliest date of publication TBC.

Questions for consultation

Have the most appropriate comparators for aflibercept for the treatment of macular oedema caused by CRVO been included in the scope?

- Should grid laser photocoagulation also be considered?
- Are the comparators listed routinely used in clinical practice?
- Should aflibercept be compared with any combination treatment?

How should 'best supportive care' be defined?

Have the most appropriate outcome measures been included in the scope? Should other outcome measures be considered?

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)