NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Brolucizumab for treating wet age-related macular degeneration

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of brolucizumab within its marketing authorisation for treating wet age-related macular degeneration.

Background

The macula is the central part of the retina responsible for colour vision and perception of fine detail. Age-related macular degeneration (AMD) refers to the deterioration in the cells of the retinal pigment layer at the macula area, which can lead to severe visual impairment in the affected eye.

Age-related macular degeneration is a common cause of vision loss in people aged over 50 years and is associated with the loss of central vision and visual distortion. There are two main types of age-related macular degeneration, wet (neovascular) and dry (non-neovascular). Wet age-related macular degeneration usually develops much more quickly than dry age-related macular degeneration and is characterised by choroidal neovascularisation, which describes the formation of immature blood vessels that grow between the retinal pigment epithelial cells and the photoreceptor cells in the centre of the retina. These new blood vessels are fragile and more likely to haemorrhage, which causes scarring of the macula leading to vision impairment. Wet AMD accounts for approximately 10% of all cases of AMD and about 60% of advanced (late stage) cases[1]. In the UK, prevalence of wet AMD is estimated to be 1.2% (2.5% in those aged 65 or above and 6.3% in those aged 80 or above) with an estimated 40,000 new cases of wet age-related macular degeneration in the UK each year[2].

The NICE guideline on age-related macular degeneration (NG82) recommends offering intravitreal anti-vascular endothelial growth factor (VEGF) treatment. Anti-VEGF medications that are licensed options for the treatment of wet AMD are ranibizumab, and aflibercept solution for injection. NICE TA155 and TA294 recommend treatment with these options when the best-corrected visual acuity is between 6/12 and 6/96, there is no permanent structural damage to the central fovea, the lesion size is less than or equal to 12 disc areas in greatest linear dimension and there is evidence of recent presumed disease progression. NG82 also recommends considering treatment for wet AMD with best-corrected visual acuity worse than 6/96 if it will benefit the person's overall visual function (e.g. it is the better-seeing eye).

The technology

Brolucizumab (brand name unknown, Novartis) is a humanised monoclonal single-chain antibody fragment which binds to vascular endothelial growth factor A (VEGF-A). This prevents the factor from stimulating the growth of fragile and permeable new blood vessels associated with wet age-related macular degeneration. It is administered by intravitreal injection.

Brolucizumab does not currently have a marketing authorisation in the UK for the treatment of neovascular (wet) age-related macular degeneration. It has been studied in clinical trials compared with aflibercept in adults with untreated active choroidal neovascularisation secondary to age-related macular degeneration.

Intervention(s)	Brolucizumab
Population(s)	Adults with untreated active choroidal neovascularisation secondary to age-related macular degeneration
Comparators	• Aflibercept • Ranibizumab • Bevacizumab (does not currently have a marketing authorisation in the UK for this indication) • Best supportive care
Outcomes	The outcome measures to be considered include: • Visual acuity (the affected eye) • Overall visual function • Central Subfield Foveal Thickness (CSFT) • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. 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 commercial arrangements for the intervention or comparator technologies will be taken into account. Cost effectiveness analysis should include consideration of the benefit in the best and worst seeing eye.
Other considerations	If the evidence allows the following subgroups will be considered: • lesion is classic or occult neovascularisation in nature. The availability and cost of biosimilar products should be taken into account. 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 only 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:** Aflibercept solution for injection for treating wet age‑related macular degeneration (2013). NICE Technology Appraisal 294. Guidance moved to static list Ranibizumab and pegaptanib for the treatment of age-related macular degeneration (2012). NICE Technology Appraisal 155. Guidance moved to static list. **Related Guidelines:** Age-related macular degeneration (2018). NICE guideline 82 Review date: None stated.

	Related Interventional Procedures: Miniature lens system implantation for advanced age-related macular degeneration (2016). NICE interventional procedures guidance 565. Epiretinal brachytherapy for wet age-related macular degeneration (2011). NICE interventional procedures guidance 415. Macular translocation with 360° retinotomy for wet age-related macular degeneration (2010). NICE interventional procedures guidance 340. Limited macular translocation for wet age-related macular degeneration (2010). NICE interventional procedures guidance 339. Transpupillary thermotherapy for age-related macular degeneration (2004). NICE interventional procedures guidance 58. Radiotherapy for age-related macular degeneration (2004). NICE interventional procedures guidance 49. **Related Quality Standards:** Serious eye disorders (in development). Publication expected February 2019 **Related NICE Pathways:** Age-related macular degeneration (2018) NICE pathway http://pathways.nice.org.uk/
Related National Policy	UK Vision Strategy 2013−2018, http://www.ukvisionstrategy.org.uk/ The Royal College of Ophthalmologists. Age-Related Macular Degeneration: Guidelines for Management. September 2013. https://www.rcophth.ac.uk/wp-content/uploads/2014/12/2013-SCI-318-RCOphth-AMD-Guidelines-Sept-2013-FINAL-2.pdf The Royal College of Optometrists and the Royal College of Ophthalmologists. Age-related macular degeneration. Commissioning better eye care - Clinical commissioning guidance. November 2013. European Society of Retina Specialists (EURETINA). Guidelines for the management of neovascular age-related macular degeneration. 2014.

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for wet age-related macular degeneration?

Should any other comparators for brolucizumab be included in the scope?

How should best supportive care be defined?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations' appropriate?

Are there any subgroups of people in whom brolucizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider brolucizumab will fit into the existing NICE pathway for age-related macular degeneration?

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 brolucizumab 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 brolucizumab 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 brolucizumab 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1 Patient Info. Age-related Macular Degeneration Available from: https://patient.info/doctor/age-related-macular-degeneration-pro

2 Owen, C.G., Jarrar, Z., Wormald, R., Cook, D.G., Fletcher, A.E. and Rudnicka, A.R. The estimated prevalence and incidence of late stage age related macular degeneration in the UK. British Journal of Ophthalmology, 2012, 96: 752-756.