NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Ranibizumab for treating diabetic retinopathy

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of ranibizumab within its marketing authorisation for treating diabetic retinopathy.

Background

Diabetic retinopathy is damage to the retina as a result of diabetes. The blood vessels in the retina can leak, become blocked or new abnormal vessels can grow. Retinopathy which affects the macula is separately described as diabetic maculopathy which includes diabetic macular oedema (DMO). There are two types of diabetic retinopathy: non-proliferative and proliferative. In non-proliferative diabetic retinopathy (NPDR) there are abnormalities in the retinal blood vessels but no formation of new vessels. NPDR can be further classified into mild, moderate, moderately severe, and severe according to the ophthalmoscopic severity of the disease. Loss of vision in NPDR is usually due to coexisting macular oedema. In proliferative diabetic retinopathy (PDR), damage to the retina stimulates the growth of new blood vessels. The new blood vessels grow abnormally, sometimes leading to haemorrhage into the eye, possible retinal detachment and loss of vision.

In 2018 there were approximately 3.8 million adults in England with diabetes, of whom 90% had type 2 diabetes. However, many people have type 2 diabetes that is undiagnosed and so the number of people with the condition may be higher than reported (it is estimated that around 900,000 people in the UK have undiagnosed diabetes). Diabetes is one of the leading causes of preventable sight loss in the UK.[1] Approximately 7.0% of the population with type 1 diabetes and 1.5% of the population with type 2 diabetes have severe or proliferative diabetic retinopathy.[2]

Management of diabetic retinopathy consists of preventive strategies to optimise blood glucose, blood lipids and blood pressure and frequent eye monitoring to pick up early signs of deterioration. The main treatment option for sight-threatening diabetic retinopathy is laser therapy (panretinal photocoagulation), in which light energy is applied to the retina with the aim of stopping the growth and development of new blood vessels, and thereby preserving vision.

The technology

Ranibizumab (Lucentis, Novartis) is a humanised recombinant monoclonal 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 marketing authorisation in the UK for treating moderately severe to severe non-proliferative and proliferative diabetic retinopathy. It has been studied in a clinical trial in people aged 18 and over with diabetic retinopathy compared with panretinal photocoagulation.

Ranibizumab has a marketing authorisation in the UK for the following related indications: treatment in adults of neovascular (wet) age-related macular degeneration, and visual impairment due to choroidal neovascularisation, diabetic macular oedema and macular oedema secondary to retinal vein occlusion.

Intervention(s)	Ranibizumab
Population(s)	• Adults with moderately severe to severe non-proliferative diabetic retinopathy • Adults with proliferative diabetic retinopathy
Comparators	For adults with moderately severe to severe non-proliferative diabetic retinopathy: - Established clinical management without ranibizumab For adults with proliferative diabetic retinopathy: - Panretinal photocoagulation
Outcomes	The outcome measures to be considered include: • Best corrected visual acuity (the affected eye) • Best corrected visual acuity (both eyes) • Progression of diabetic retinopathy • 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 commercial arrangements for the intervention, comparator and subsequent treatment 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, consideration will be given to subgroups according to the stage of diabetic retinopathy. 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: Ranibizumab for treating diabetic macular oedema (2013). NICE Technology appraisal guidance 274. Aflibercept for treating diabetic macular oedema (2015). NICE Technology appraisal guidance 346. Dexamethasone intravitreal implant for treating diabetic macular oedema (2015). NICE Technology appraisal guidance 349. Fluocinolone acetonide intravitreal implant for treating chronic diabetic macular oedema after an inadequate response to prior therapy (2013). NICE Technology appraisal guidance 301. Related Guidelines: Type 1 diabetes in adults: diagnosis and management (2015). NICE guideline 17. Last updated July 2016. Type 2 diabetes in adults: management (2015). NICE guideline 28. Last updated May 2017.
Related National	The NHS Long Term Plan, 2019. NHS Long Term Plan

Policy	NHS England. 2013/14 NHS Standard Contract for Ophthalmic Pathology Service (All Ages). D12/S(HSS)/b. NHS England (2018) NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year Forward View' Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

What proportion of people with moderately severe to severe non-proliferative diabetic retinopathy and proliferative diabetic retinopathy, who are eligible for panretinal photocoagulation, are also eligible for intravitreal VEGF inhibitors due to coexisting diabetic macular oedema?

Where do you consider ranibizumab would fit into the existing treatment pathway for moderately severe to severe non-proliferative diabetic retinopathy and proliferative diabetic retinopathy?

What is the clinical evidence supporting the use of ranibizumab in moderately severe to severe non-proliferative diabetic retinopathy?

Have all relevant comparators for ranibizumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for treating moderately severe to severe non-proliferative diabetic retinopathy and proliferative diabetic retinopathy?

- Do the comparators differ for moderately severe to severe non-proliferative diabetic retinopathy, and for proliferative diabetic retinopathy? Is panretinal photocoagulation also used to treat moderately severe to severe non-proliferative diabetic retinopathy?

- Are other intravitreal VEGF inhibitors (e.g. aflibercept and bevacizumab) currently used in the NHS for treating moderately severe to severe non-proliferative diabetic retinopathy and proliferative diabetic retinopathy?

- What is the place of vitreoretinal surgery in the management of moderately severe to severe non-proliferative diabetic retinopathy and proliferative diabetic retinopathy?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate? Are there any subgroups of people in whom ranibizumab is expected to be more clinically effective or 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 ranibizumab 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 ranibizumab 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 ranibizumab 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).

References

1 Diabetes UK (2019) 'Diabetes: Facts and Stats'. Accessed May 2019.

2 Mathur R, Bhaskaran K, Edwards E, Lee H, Chaturvedi N, Smeeth L, et al. Population trends in the 10-year incidence and prevalence of diabetic retinopathy in the UK: a cohort study in the Clinical Practice Research Datalink 2004–2014. BMJ Open. 2017;7(2).