NICE National Institute for Health and Care Excellence

NICE guidance

Aflibercept for treating choroidal neovascularisation

Technology appraisal guidance

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nice.org.uk/guidance/ta486

Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance are at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Aflibercept is recommended, within its marketing authorisation, as an option for treating visual impairment because of myopic choroidal neovascularisation in adults, only if the company provides aflibercept with the discount agreed in the patient access scheme.

1.2 If patients and their clinicians consider both aflibercept and ranibizumab to be suitable treatments, the least costly should be used, taking into account anticipated administration costs, dosage and price per dose.

Why the committee made these recommendations

Ranibizumab is already recommended by NICE for treating choroidal neovascularisation. An indirect comparison of aflibercept and ranibizumab shows that both drugs provide similar overall health benefits. The total costs of aflibercept are the same as or less than those of ranibizumab.

Because it is has similar costs and overall health benefits to ranibizumab, aflibercept is also recommended as a cost-effective option for treating choroidal neovascularisation.

2 The technology

Aflibercept (Eylea, Bayer)	
Marketing authorisation	Aflibercept has a UK marketing authorisation for 'treating visual impairment due to myopic choroidal neovascularisation in adults'.
Recommended dose and schedule	The recommended dose is a single intravitreal injection of 2 mg aflibercept (equivalent to 50 microlitres). Extra doses may be used if visual or anatomic outcomes indicate that the disease persists. Recurrences should be treated as a new manifestation of the disease. For full details, see the summary of product characteristics.
Price	The list price of aflibercept 40 mg/mL is £816 per 0.1-mL vial (excluding VAT; British national formulary [BNF] online [accessed July 2017]). The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of aflibercept, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence. The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS.

3 Committee discussion

The appraisal committee (section 5) considered evidence submitted by Bayer and a review of this submission by the evidence review group (ERG). See the committee papers for full details of the evidence.

Aflibercept compared with ranibizumab

The comparison of aflibercept and ranibizumab is appropriate

3.1 NICE has already produced technology appraisal guidance on ranibizumab in this indication. The company presented a cost comparison case, in which it proposed that:

- the overall health benefits associated with aflibercept are similar to or greater than those associated with ranibizumab
- the total costs associated with aflibercept are similar to or lower than those associated with ranibizumab.

The committee understood that treatment with ranibizumab is the standard of care for choroidal neovascularisation in the NHS. The committee concluded that it was appropriate for the company to compare aflibercept with ranibizumab.

Clinical effectiveness

Aflibercept and ranibizumab are similarly effective in treating choroidal neovascularisation

3.2 The company presented an indirect treatment comparison comparing mean change in best corrected visual acuity with aflibercept and ranibizumab at 3 months. This used data from 3 trials: the MYRROR and RADIANCE randomised controlled trials of aflibercept and ranibizumab respectively, which were linked by the VIP trial of verteporfin photodynamic therapy and placebo. The committee was concerned that VIP was relatively old and included neither aflibercept nor ranibizumab. It was also concerned that the indirect comparison was based on a small number of patients, because there were only 31 patients in the placebo arm of MYRROR. The committee noted that the difference in retreatment criteria between the trials made it difficult to compare them.

Retreatment in MYRROR was guided by a combination of both disease activity and visual acuity, whereas in RADIANCE there were 2 separate ranibizumab retreatment arms, 1 based on visual acuity and the other based on disease activity. Mean change in best corrected visual acuity for aflibercept compared with ranibizumab was 1.34 letters using the visual acuity retreatment arm (95% confidence interval [CI] −5.35 to 8.00) and 0.94 using the disease activity retreatment arm (95% CI −5.67 to 7.56). The committee understood from the clinical expert and patient and professional organisations that in clinical practice, aflibercept is considered to be slightly more effective than ranibizumab. It concluded that despite uncertainties in the indirect treatment comparison, aflibercept is as effective as ranibizumab in treating choroidal neovascularisation.

Adverse events

Adverse events with aflibercept are likely to be similar to those with ranibizumab

3.3 The committee understood that the only direct evidence comparing the rates of adverse events with aflibercept and ranibizumab was from a clinical trial in wet age-related macular degeneration, which showed that they were similar. The ERG confirmed that the types and rates of adverse events in MYRROR and RADIANCE also seem to be similar, although it is not possible to link the trials together for an indirect comparison. The committee concluded that the adverse events associated with aflibercept were likely to be similar to those associated with ranibizumab when treating choroidal neovascularisation.

Overall health benefits

Aflibercept provides similar overall health benefits to ranibizumab

3.4 The committee concluded that because both the gain in best corrected visual acuity and adverse events with aflibercept and ranibizumab were similar, the treatments were also likely to provide similar overall health benefits.

Resource use

It is appropriate to assume the same number of aflibercept and ranibizumab injections

3.5 The company assumed the same number of aflibercept and ranibizumab injections in the first year, based on the mean number in the MYRROR trial. Its rationale was that the confidence intervals for the mean number of injections in MYRROR and the 2 arms of RADIANCE overlapped, and that market research suggested that the retreatment criteria in MYRROR best reflected clinical practice in England. The ERG explained that the retreatment criteria in MYRROR were more similar to the disease activity retreatment arm of RADIANCE than the visual acuity retreatment arm. The committee was concerned that because the mean number of injections in the disease activity retreatment arm of RADIANCE was lower than the mean number of injections in MYRROR (3.5 compared with 4.2), assuming equal injection frequency may underestimate the costs associated with aflibercept. However, it noted comments from the clinical expert and patient and professional organisations that it takes the same number of injections with both aflibercept and ranibizumab to stabilise the disease. Some comments suggested that fewer injections are needed with aflibercept compared with ranibizumab. Having considered the evidence, the committee agreed that it was appropriate to assume the same number of injections with both aflibercept and ranibizumab.

Cost comparison results

Aflibercept meets the criteria for a successful cost comparison

3.6 The committee considered the company's cost comparison, which assumed equal injection frequency and included all patient access schemes. The results showed that the total costs associated with aflibercept are similar to or lower than those associated with ranibizumab (the exact results cannot be reported here because the discounts are confidential). The committee concluded that the criteria for a positive cost comparison were met, because:

- the overall health benefits associated with aflibercept were similar to or greater than the overall health benefits associated with ranibizumab

- the total costs associated with aflibercept were similar to or lower than the total costs associated with ranibizumab.

The committee therefore recommended aflibercept as a cost-effective use of NHS resources for treating visual impairment because of myopic choroidal neovascularisation in adults.

4 Implementation

4.1 Section 7(6) of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication. Because aflibercept has been recommended through the fast track appraisal process, NHS England and commissioning groups have committed to providing funding to implement this guidance 30 days after publication.

4.2 The Welsh Ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal determination.

4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has choroidal neovascularisation and the doctor responsible for their care thinks that aflibercept is the right treatment, it should be available for use, in line with NICE's recommendations.

4.4 The Department of Health and Bayer have agreed that aflibercept will be available to the NHS with a patient access scheme which makes it available with a discount. The size of the discount is commercial in confidence. It is the responsibility of the company to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about the patient access scheme should be directed to access.team@bayer.com.

5 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee C.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Ross Dent
Technical lead

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Accreditation