NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Technology Appraisal Review Proposal paper

Review of TA305; Aflibercept for treating visual impairment caused by macular oedema secondary to central retinal vein occlusion

Original publication date:	February 2014
Review date	February 2017
Existing recommendations:	Recommended To see the complete existing recommendations and the original remit for TA305, see Appendix A.

1. Proposal

The guidance should be transferred to the 'static guidance list'. That we consult on this proposal.

2. Rationale

Since the publication of TA305, no significant new evidence has been identified that is likely to lead to a change in the current guidance. It is therefore appropriate to transfer this guidance to the 'static guidance list'.

3. Summary of new evidence and implications for review

Has there been any change to the price of the technology since the guidance was published?
The list price of aflibercept has not changed since the publication of TA305. The company has agreed a confidential patient access scheme with the Department of Health that provided a simple discount to the list price of aflibercept. There is no indication of a further discount being provided for aflibercept.
Are there any existing or proposed changes to the marketing authorisation that would affect the existing guidance?
There are no existing proposed changes to the marketing authorisation.
Were any uncertainties identified in the original guidance? Is there any new evidence that might address this?

In TA305 there was some uncertainty around the different definitions of ischaemia and severe ischaemia that exist, therefore it was unclear whether any evidence had been presented for people with ischaemia or severe ischaemia. No new evidence is viable for people with ischaemia or severe ischaemia. There was some uncertainty about the clinical effectiveness of aflibercept compared with ranibizumab and dexamethasone. The committee concluded that there was no evidence that aflibercept was not as clinically effective as ranibizumab or dexamethasone. The literature review identified 1 study (Krivasi *et al*, 2016) that showed that aflibercept was more effective then dexamethasone at 24 weeks. It also presented results of aflibercept against ranibizumab but these results were inconclusive. The results of this study have no implications for existing guidance.
Are there any related pieces of NICE guidance relevant to this appraisal? If so, what implications might this have for the existing guidance?
NICE has since published guidance on aflibercept for treating visual impairment caused by macular oedema after branch retinal vein occlusion (TA409). However, this does not have any implications on the existing guidance. *See Appendix C for a list of related NICE guidance.*
Additional comments
None

The search strategy from the original ERG report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from January, 2013 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix C for further details of ongoing and unpublished studies.

4. Equalities issues

No equality and diversity issues were raised in the original guidance.

GE paper sign off: Meindert Boysen, 01 February 2017

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Appendix A – Information from existing guidance

5. Original remit

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

6. Current guidance

Aflibercept solution for injection is recommended as an option for treating visual impairment caused by macular oedema secondary to central retinal vein occlusion only if the manufacturer provides aflibercept solution for injection with the discount agreed in the patient access scheme.

7. Research recommendations from original guidance

N/A

8. Cost information from original guidance

The list price of aflibercept 40 mg/ml solution for injection is £816.00 per 0.1-ml vial (excluding VAT; 'British national formulary' [BNF] edition 66). The manufacturer of aflibercept solution for injection has agreed a patient access scheme with the Department of Health which makes aflibercept solution for injection available with a discount applied to the list price.

Appendix B – Explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	**Consequence**	**Selected – 'Yes/No'**
A review of the guidance should be planned into the appraisal work programme. The review will be conducted through the specify STA or MTA process.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred to specify date or trial.	NICE will reconsider whether a review is necessary at the specified date.	No
A review of the guidance should be combined with a review of a related technology appraisal. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No

Appendix B

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going clinical guideline[1].	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes
The guidance should be withdrawn	The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS. The guidance will be stood down and any funding direction associated with a positive recommendation will not be preserved.	No

[1] Information on the criteria for NICE allowing a technology appraisal in an ongoing clinical guideline can be found in section 6.20 of the guide to the processes of technology appraisal.

Appendix C – other relevant information

1. Relevant Institute work

Published

Technology appraisal guidance [TA229] Dexamethasone intravitreal implant for the treatment of macular oedema secondary to retinal vein occlusion. Published date: July 2011. Review date: January 2015. Review decision: Moved to static list

Technology appraisal guidance [TA409] Aflibercept for treating visual impairment caused by macular oedema after branch retinal vein occlusion. Published date: September 2916. Review date: October 2019

Technology appraisal guidance [TA283] Ranibizumab for treating visual impairment caused by macular oedema secondary to retinal vein occlusion. Published date: May 2013. Review date: March 2016. Review decision: Moved to static list

2. Details of changes to the indications of the technology

Indication and price considered in original appraisal	Proposed indication (for this appraisal) and current price
'The treatment of visual impairment due to macular oedema secondary to central retinal vein occlusion (CRVO)'. The list price of aflibercept 40 mg/ml solution for injection is £816.00 per 0.1-ml vial (excluding VAT; 'British national formulary' [BNF] edition 66).	No change in price or indication Aflibercept 40 mg/mL, net price 0.1-mL vial = £816.00 (BNF November 2016)

3. Details of new products

Drug (company)	Details (phase of development, expected launch date)	In topic selection
N/A	N/A	N/A

4. Registered and unpublished trials

Trial name and registration number	Details
A Multi-center, Single-arm, Interventional Phase 4 Study to Evaluate a Treat and Extend Regimen of Intravitreal Aflibercept for Treatment of Macular Edema Secondary to Central Retinal Vein Occlusion (NCT02800642)	Estimated Enrolment: 160 Estimated Study Completion Date: August 2019 This study is currently recruiting participants.
Suprachoroidal Injection of Triamcinolone Acetonide With IVT Aflibercept in Subjects With Macular Edema Following RVO (SAPPHIRE) (NCT02980874)	Estimated Enrolment: 460 Estimated Study Completion Date: June 2019 This study is not yet open for participant recruitment.
Study of COmparative Treatments for REtinal Vein Occlusion 2 [SCORE2]: a Multicenter, Prospective, Randomized Non-inferiority Trial of Eyes With Macular Edema Secondary to Central Retinal Vein Occlusion, Comparing Intravitreal Bevacizumab Every 4 Weeks With Intravitreal Aflibercept Every 4 Weeks.(NCT01969708)	Enrolment: 362 Estimated Study Completion Date: March 2019 This study is ongoing, but not recruiting participants.
Randomized Trial Comparing Injection Frequency Between Aflibercept and Ranibizumab in Patients With Central Retinal Vein Occlusion With a Treat and Extend Algorithm (NCT02274259)	This study is ongoing, but not recruiting participants Estimated Enrolment: 40 Estimated Study Completion Date: December 2016

5. Additional information

Bayer intend to continue the current patient access scheme which is in place for aflibercept without changes.