NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA283; Ranibizumab for treating visual impairment caused by macular oedema secondary to retinal vein occlusion

This guidance was issued in May 2013.

The review date for this guidance is March 2016.

1. Recommendation

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

2. Original remit(s)

To appraise the clinical and cost effectiveness of ranibizumab within its licensed indication for the treatment of macular oedema caused by retinal vein occlusion (RVO).

3. Current guidance

1.1 Ranibizumab is recommended as an option for treating visual impairment caused by macular oedema:

- following central retinal vein occlusion or
- following branch retinal vein occlusion only if treatment with laser photocoagulation has not been beneficial, or when laser photocoagulation is not suitable because of the extent of macular haemorrhage and
- only if the manufacturer provides ranibizumab with the discount agreed in the patient access scheme revised in the context of NICE technology appraisal guidance 274.

1.2 People currently receiving ranibizumab whose disease does not meet the criteria in 1.1 should be able to continue treatment until they and their clinician consider it appropriate to stop.

4. Rationale[1]

[1] A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper

No new studies were identified that would materially impact the current recommendations.

5. Implications for other guidance producing programmes

There is no proposed or ongoing guidance development that overlaps with this review proposal

6. New evidence

The search strategy from the original ERG report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from January 2011 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 See Appendix 2 for further details of ongoing and unpublished studies.

7. Summary of evidence and implications for review

Since the publication of TA 283, the marketing authorisation for ranibizumab has not changed with respect to the indication considered as part of the technology appraisal. There have been no price changes to ranibizumab since publication of TA283. However, aflibercept has since received a marketing authorisation for macular oedema secondary to central retinal vein occlusion (CRVO) and was recommended in TA 305 (February 2014) as an option for treating visual impairment caused by macular oedema secondary to CRVO only if the manufacturer provides aflibercept solution for injection with the discount agreed in the patient access scheme for where it was recommended as an option. Aflibercept has more recently received a marketing authorisation for macular oedema secondary to branch retinal vein occlusion (BRVO) – in February 2015 – and is currently subject to an appraisal (ID844).

Fifty-eight studies were identified by the bibliographic searches. Several systematic reviews were identified which supported recommendations in TA283. A randomised controlled study was identified which compared intravitreal bevacizumab with ranibizumab for macular oedema caused by branch retinal vein occlusion (MARVEL) which suggested significant gain in visual acuity in eyes with BRVO treated with either bevacizumab or ranibizumab. A clinical trial comparing the two drugs (NCT01635803) which concludes in July 2016 and which looks at both clinical and cost effectiveness could be of interest. However, it is worth noting that during the appraisal of aflibercept (TA305), the committee heard from clinical experts that the use of bevacizumab has decreased since the publication of NICE's guidance on ranibizumab (NICE technology appraisal guidance 283) and dexamethasone (NICE technology appraisal guidance 229). In light of the unlicensed status of bevacizumab and decreased use in clinical practice this may not be enough justification for a deferral of a review of the guidance.

There were no studies identified in the literature searches which could materially impact upon the current recommendations.

8. Adoption and Impact

No submission was received from the Adoption and Impact team.

9. Equality issues

None identified in the original guidance.

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Appendix 1 – 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

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going clinical guideline.	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

NICE would typically consider updating a technology appraisal in an ongoing guideline if the following criteria were met:

i. The technology falls within the scope of a clinical guideline (or public health guidance)

ii. There is no proposed change to an existing Patient Access Scheme or Flexible Pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement

iii. There is no new evidence that is likely to lead to a significant change in the clinical and cost effectiveness of a treatment

iv. The treatment is well established and embedded in the NHS. Evidence that a treatment is not well established or embedded may include;

- Spending on a treatment for the indication which was the subject of the appraisal continues to rise
- There is evidence of unjustified variation across the country in access to a treatment
- There is plausible and verifiable information to suggest that the availability of the treatment is likely to suffer if the funding direction were removed

- The treatment is excluded from the Payment by Results tariff

v. Stakeholder opinion, expressed in response to review consultation, is broadly supportive of the proposal.

Appendix 2 – supporting information

Relevant Institute work

Published

Aflibercept for treating visual impairment caused by macular oedema secondary to central retinal vein occlusion (2014) NICE technology appraisal guidance 305 Review date: February 2017

Dexamethasone intravitreal implant for the treatment of macular oedema secondary to retinal vein occlusion (2011) NICE technology appraisal guidance 229 Review date: January 2015 - moved to static list.

In progress

Macular oedema (branch retinal vein occlusion) - aflibercept [ID844] Technology appraisal. Publication expected October 2016

Suspended/terminated

Macular oedema (diabetic) - pegaptanib sodium [ID452] Technology appraisal. Suspended (NICE has been informed by the manufacturer of Pegaptanib, Pfizer, that they have withdrawn their licensing application for the above indication.)

Details of new products

Drug (company)	Details (phase of development, expected launch date)	In topic selection
Aflibercept (Bayer)	Aflibercept for the treatment of visual impairment due to macular oedema secondary to branch retinal vein occlusion (BRVO) received marketing authorisation in February 2015. The CRVO indication received its MA in September 2013.	ID844, Aflibercept for the treatment of visual impairment due to macular oedema secondary to BRVO technology appraisal in development. 1st committee meeting 11th May 2016. Technology appraisal guidance for aflibercept for the treatment of visual impairment due to macular oedema secondary to CRVO was published in February 2014

Registered and unpublished trials

Trial name and registration number	Details
Ranibizumab for Macular Edema Secondary to Branch Retinal Vein Occlusion in Patients With Fair Vision (RVOFV) (NCT01795209)	Enrolment: 19 Estimated Study Completion Date: July 2016 This study is ongoing, but not recruiting participants.
Evaluation of the Usefulness of a PRN Regimen Using Ranibizumab for Macular Edema Due to Branch Retinal Vein Occlusion (NCT02478515)	Estimated Enrolment: 30 Estimated Study Completion Date: September 2017 This study is currently recruiting participants.
Ranibizumab Intravitreal Injections Versus Sham Control in Patients With Branch Retinal Vein Occlusion (BRVO) (Blossom) (NCT01976338)	Enrolment: 283 Estimated Study Completion Date: April 2016 This study is ongoing, but not recruiting participants.

Trial name and registration number	Details
Ranibizumab Intravitreal Injections Versus Sham Control in Patients With Central Retinal Vein Occlusion (CRVO) (Camellia) (NCT01976312)	Enrolment: 252 Estimated Study Completion Date: March 2016
Efficacy and Safety of Ranibizumab With or Without Laser in Comparison to Laser in Branch Retinal Vein Occlusion (BRIGHTER) (NCT01599650)	Enrolment: 455 Study Completion Date: May 2015 This study has been completed.
Comparing the Effectiveness and Costs of Bevacizumab to Ranibizumab in Patients With Retinal Vein Occlusions (BRVO) (NCT01635803)	Estimated Enrolment: 296 Estimated Primary Completion Date: June 2016 This study is currently recruiting participants
Evaluation of the "Treat-and-extend" Scheme in Patients With Retinal Vein Occlusion (RVO) With and Without LASER Treatment of Ischaemic Retinal Areas (PEARL) (NCT02522897)	Estimated Enrolment: 60 Estimated Study Completion Date: January 2018 This study is not yet open for participant recruitment
Comparing Injection Frequency Between Aflibercept and Ranibizumab in Patients With CRVO With a Treat& Extend Regimen (NCT02274259)	Estimated Enrolment: 40 Estimated Study Completion Date: December 2016 This study is currently recruiting participant

Additional information

The price of ranibizumab is unchanged since TA283 was published in May 2013. Lucentis 2.3mg/0.23ml solution for injection vials – 1 vial £742.00