NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA301; Fluocinolone acetonide intravitreal implant for treating chronic diabetic macular oedema after an inadequate response to prior therapy

This guidance was issued in November, 2013

The review date for this guidance is November, 2016

1. Recommendation

A part-review and part re-issue of the guidance should be planned into the appraisal work programme. For those people within the marketing authorisation with phakic lenses, for whom fluocinolone is not recommended in TA301. The part-review will be conducted through the STA process.

For those people with pseudophakic lenses where fluocinolone is already recommended in TA301, a re-issue of these, unchanged, positive recommendations, accounting for the new PAS is suggested.

2. Original remit(s)

To appraise the clinical and cost effectiveness of fluocinolone acetonide intravitreal implant within its licensed indication for the treatment of diabetic macular oedema.

3. Current guidance

1.1 Fluocinolone acetonide intravitreal implant is recommended as an option for treating chronic diabetic macular oedema that is insufficiently responsive to available therapy(ies) only if:

- the implant is to be used in an eye with an intraocular (pseudophakic) lens; and
- the manufacturer provides fluocinolone acetonide intravitreal implant with the discount agreed in the patient access scheme.

Fluocinolone acetonide intravitreal implant has a marketing authorisation for 'the treatment of vision impairment associated with chronic diabetic macular oedema considered insufficiently responsive to available therapies'.

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

The company in its response to the review proposal has indicated that there is new evidence supporting the clinical and cost effectiveness of fluocinolone acetonide for the full licenced population. Currently, fluocinolone acetonide is only recommended by NICE for people who have implanted intraocular lenses. The new evidence would support the use of fluocinolone acetonide in people with phakic lenses.

[redacted] will impact on the cost-effectiveness of both the subgroups for which fluocinolone acetonide is not currently recommended and that for which fluocinolone acetonide is currently recommended, a part STA review of TA301 for those groups not recommended in TA301 should be considered. For those groups with pseudophakic lenses where fluocinolone is already recommended a re-issue of the positive recommendations is suggested. The positive recommendations remain unchanged, [redacted].

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 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 2 for further details of ongoing and unpublished studies.

7. Summary of evidence and implications for review

There are no changes to the current marketing authorisation and none are expected in the next 3 years. Nor have there been any changes in the marketing authorisation for its comparators.

A new treatment for DMO, danazol (Ampio) is currently in NICE topic selection (ID 8124). Another is currently in phase 2 studies.

There is one retrospective long-term study of outcomes in people with diabetic macular oedema treated with intravitreal fluocinolone acetonide implants whose lenses are phakic (Yang 2015). This study analysed the phase 3 FAME safety and efficacy data of fluocinolone acetonide implants in patients who underwent cataract extraction before implant or cataract extraction after implant. The results suggest that best corrected visual acuity after 36 months was comparable in both groups.

[redacted]

It is unclear whether the data will likely lead to a change in the recommendation without further details of the health economic models the company is working on to present to NICE.

8. Adoption and Impact

A submission from the Adoption and Impact team is included in Appendix 3.

The implementation report suggests that the use of fluocinolone acetonide is only prescribed in secondary care and steadily increased since NICE technology appraisal 301 was published. However, the since NICE technology appraisal 349 (Dexamethasone intravitreal implant for treating diabetic macular oedema) and 346 (Aflibercept for treating diabetic macular oedema) were given positive recommendations, the uptake of fluocinolone acetonide has decreased by one-third (from approximately £1.2 million in quarter 1 of 2015 to £850,000 in quarter 3 of that same year.

9. Equality issues

No equality issues have been identified by the committee in TA271 or the rapid review TA301.

GE paper sign off: Frances Sutcliffe, Associate Director, 27/07/2017

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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 part-review of the guidance should be planned into the appraisal work programme. The part-review will be conducted through the STA process.	A part-review and a part-reissue of the appraisal will be planned into the NICE's work programme.	Yes
The decision to review the guidance should be deferred to a specific 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.	No
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

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

Technology appraisal guidance [TA346] Aflibercept for treating diabetic macular oedema Published: 22 July 2015. Review date: July 2018

Technology appraisal guidance [TA349] Dexamethasone intravitreal implant for treating diabetic macular oedema Published: 22 July 2015. Review date: July 2018

Technology appraisal guidance [TA274] Ranibizumab for treating diabetic macular oedema Published: 27 February 2013. Review date: April 2015 - transferred to static list.

Suspended/terminated

Macular oedema (diabetic) - pegaptanib sodium [ID452] In development [GID-TAG280] Expected publication date: TBC (NICE has been informed by the manufacturer of Pegaptanib, Pfizer, that they have withdrawn their licensing application for the above indication. Therefore this appraisal topic has been suspended).

Details of changes to the indications of the technology

Indication and price considered in original appraisal	Proposed indication (for this appraisal) and current price
Price: 190-micrgram implant at a price of £5,500 (excluding VAT) Source: TA301	[redacted] Current price: 190-micrgram implant at a price of £5,500 (excluding VAT) Source: BNF September 2016

Details of new products

Drug (company)	Details (phase of development, expected launch date)	Post topic selection
Danazol (Optina; Vasaloc) (Ampio Pharmaceuticals Inc.)	Phase III trial completed	Topic selection ID: 8124 Topic prioritised for potential technology appraisal guidance production. Topic passed to scoping team to prepare for a consultation exercise
Luminate (Allegro Ophthalmics, LLC)	Currently recruiting for a phase II trial	

Registered and unpublished trials

Trial name and registration number	Details
A Non-randomised, Open-label, Multicenter Phase 4 Pilot Study on the Effect and Safety of Iluvien® in Chronic Diabetic Macular Edema Patients Considered Insufficiently Responsive to Available Therapies With or Without Intravitreal Corticosteroid Therapy (RESPOND) NCT02359526	Phase 4 trial Estimated Enrolment: 12 Estimated Study Completion Date: December 2016
Fluocinolone Acetonide Insert (ILUVIEN®) for Diabetic Macular Edema (FAD) Study NCT02902744	Phase 4 trial Estimated Enrolment: 50 Estimated Primary Completion Date: September 2018
A Phase 4 Safety Study of IOP Signals in Patients Treated With ILUVIEN® (Fluocinolone Acetonide Intravitreal Implant) 0.19 mg NCT02424019	Phase 4 trial Estimated Enrolment: 300 Estimated Study Completion Date: April 2019

References

Yang, Y (2015) **Long-term outcomes of phakic patients with diabetic macular oedema treated with intravitreal fluocinolone acetonide (FAc) implants.** *Eye* 29 (9) 1173-1180**.**

Appendix 3 – Adoption and Impact submission

Please contact Louise Miller regarding any queries louise.miller@nice.org.uk

1. Routine healthcare activity data

1.1 ePACT data

No data relating to fluocinolone acetonide was available. This medicine appears to be prescribed only in secondary care.

[redacted]

[redacted]

2. Implementation studies from published literature

Our uptake database does not hold any information for this medicine.

3. Implementation studies from shared learning

No shared learning examples have been submitted for this guidance.

Healthcare activity data definitions

IMS HEALTH Hospital Pharmacy Audit Index

IMS HEALTH collects information from pharmacies in hospital trusts in the UK. The section of this database relating to England is available for monitoring the overall usage in drugs appraised by NICE. The IMS HPAI database is based on issues of medicines recorded on hospital pharmacy systems. Issues refer to all medicines supplied from hospital pharmacies to: wards; departments; clinics; theatres; satellite sites and to patients in outpatient clinics and on discharge.

Measures of prescribing

Volume: The HPAI database measures volume in packs and a drug may be available in different pack sizes and pack sizes can vary between medicines.

Cost: Estimated costs are also calculated by IMS using the drug tariff and other standard price lists. Many hospitals receive discounts from suppliers and this is not reflected in the estimated cost.

Costs based on the drug tariff provide a degree of standardization allowing comparisons of prescribing data from different sources to be made. The costs stated in this report do not represent the true price paid by the NHS on medicines. The estimated costs are used as a proxy for utilization and are not suitable for financial planning.

Data limitations

IMS HPAI data do not link to demographic or to diagnosis information on patients. Therefore, it cannot be used to provide prescribing information on age and sex or for prescribing of specific conditions where the same drug is licensed for more than one indication.