Dear National Institute for Health and Care Excellence

RE: Appraisal consultation document for 'Aflibercept (AFLIBER) for treating diabetic macular oedema (DMO) [reference, ID717]'

Alimera Sciences Limited is the marketing authorisation holder of ILUVIEN® (fluocinolone acetonide 190µg intravitreal [FAc] implant) which is indicated for the treatment of vision impairment associated with chronic DMO, considered insufficiently responsive to available therapies.[1] This was approved by NICE in November 2013 in technology appraisal guidance TA301[2], which stipulated that ILUVIEN should be used in patients with a pseudophakic lens, and under the agreed patient access scheme. This effectively positions ILUVIEN as a second line treatment and can be considered for this patient group irrespective of the thickness of the fovea.

The appraisal committee requested feedback for AFLIBER for treating diabetic macular oedema and Alimera Sciences would like to raise key considerations relating to the clinical application of AFLIBER.

Clinical application of AFLIBER

1. No option for patients with a central retinal thickness less than 400 micrometres
AFLIBER is being recommended as an option for treating visual impairment caused by DMO only if:

a. The eye has a central retinal thickness of 400 micrometres or more at the start of treatment; and
b. The company provides AFLIBER with the discount agreed in the patient access scheme.

In effect this means that patients with a central retinal thickness less than 400 micrometres will not have access to a first-line therapy. This means that these patients will be denied treatment until their disease has progressed to a stage where permanent damage to the eye has already begun.[3]

2. Watch and wait is not a therapy for DMO
In effect, by ignoring this group of patients, NICE is encouraging clinicians to adopt a 'watch and wait' therapy (i.e., no active treatment received). We would like to highlight that 'watch and wait' is not a standard of care (SOC) for patients with DMO and potentially detrimental to a patient's outcome, with reports claiming that nearly half of the patients developing DMO lose two or more lines of visual acuity within 2 years.[4]

3. There is an evidence base to support the use of AFLIBER in patients where central retinal thickness is less than 400 micrometres

Furthermore, the current evidence,[5] shows that intravitreous AFLIBER, bevacizumab, and ranibizumab improved vision in eyes with center-involved DMO but the relative effect depended on baseline visual acuity. When the initial visual-acuity loss was mild (visual acuity between 20/32 and 20.40 at baseline), there were no apparent differences, on average, among study groups. At worse levels of initial visual acuity (20/50 or worse at baseline), AFLIBER was more effective at improving vision (please see www.ClinicalTrials.gov; trial number, NCT01627249). However, the data for the mild visual-acuity loss shows that AFLIBER was effective with central subfield thickness decreasing from 373±108 (mean±SD) at baseline to 242±57 micrometres after one year (mean change of -129±110 micrometres).[5] This clearly shows the AFLIBER was effective in a group where mean central subfield thickness was less than 400 micrometres.

4. There is no evidence base to support switching between anti-VEGF therapies

No data was presented in the above report to suggest that switching between anti-VEGF therapies would be an effective strategy as a first-line therapy for the management of DMO. Hence, based on this trial where visual acuity was taken into account, AFLIBER would be the logical first choice in patients with a central subfield thickness less than and greater than 400 microns.

Alimera Sciences would very much like the appraisal committee to comment on these important considerations at the Appraisal Committee on 24th March 2015.

Yours sincerely

References

1. Summary of Product Characteristics (SmPC) for ILUVIEN 190 micrograms intravitreal implant in applicator. Source: https://www.medicines.org.uk/emc/medicine/27636 Published 18th February 2015.
2. FiercePharma. NICE gives EYLEA a provisional green light to treat patients with visual impairment due to DMO. Published 19th February 2015. Source. http://www.fiercepharma.com/press-releases/nice-gives-eylea-provisional-green-light-treat-patients-visual-impairment-d
3. NICE technology appraisal guidance [TA301] published November 2013. Appraisal 301. Source: http://www.nice.org.uk/guidance/ta301/documents
4. Ciulla TA et al. Treatment of diabetic macular edema with sustained-release glucocorticoids: intravitreal triamcinolone acetonide, dexamethasone implant, and fluocinolone acetonide implant. Expert Opinion on Pharmacotherapy 2014; 15 (7): 953-959. Source: http://informahealthcare.com/doi/abs/10.1517/14656566.2014.896899).
5. The Diabetic Retinopathy Clinical Research Network. Aflibercept, Bevacizumab, or Ranibizumab for Diabetic Macular Edema. N Engl J Med. 2015 Feb 18. [Epub ahead of print].