Royal College of Ophthalmologists comments on:

Fluocinolone acetonide intravitreal implant for treating chronic diabetic macular oedema after an inadequate response to prior therapy (rapid review of technology appraisal 271)

- Has all of the relevant evidence been taken into account?
- All the relevant evidence from FAME trials have been used. Primary endpoint data as well as subgroup analysis and also patient reported outcome data analyses were used to evaluate cost effectiveness.

- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- It is beyond my remit to comment in detail on the summary of cost effectiveness.
- Regarding clinical effectiveness, (section 4.6) the committee felt that subgroup of patients who were unresponsive to other therapies were somewhat different to the population with chronic DMO as defined by the subgroup analysis from the FAME studies because study eyes did not have prior therapy with Anti-VEGF, only laser photocoagulation. As corticosteroids are believed to have an antiVEGF effect, the committee felt that the level of response to Iluvien could be less if used in patients who have not been responsive to ranibizumab.
- I feel that although this is a logical assumption, there is little evidence to support the hypothesis that patients who are unresponsive to antiVEGF would also be unresponsive to corticosteroids. Indeed there are numerous clinical studies using off-label therapies showing that intravitreal corticosteroid such as triamcinolone had a strong effect on resolution of macular oedema in cases where avastin have not been efective. Several basic science studies showing that in one third of eyes with DMO, VEGF levels are not elevated compared to controls and antiVEGF therapy may be futile in those cases. Furthermore, the effect of corticosteroid on suppressing VEGF is very weak as patients with ischaemic retinal vein occlusion still develop iris neovascularisation and neovascular glaucoma(VEGF driven complications which respond well to anti VEGF).
- In my opinion, current evidence is tending to suggest that there will be a significant proportion of eyes with DMO that will be unresponsive to anti VEGF and switching to a long acting corticosteroid with a better safety profile than triamcinolone can be expected to give additional treatment response.

- It is reasonable to consider switching to intravitreal fluocinolone especially if there is minimal response to antiVEGF, rather than continuing with multiple antivegf therapy which is futile.
- Are the provisional recommendations sound and a suitable basis for guidance to theN HS?
- Yes – it is very sensible to target those patients who are pseudophakic in the first instance.
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?
- NO