Use of Bevacizumab in Wet Age Related Macular Degeneration (AMD)
GMMMG Clinical Recommendation
November 2015

At its meeting on the 19th November 2015 the Greater Manchester Medicines Management Group (GMMMG) re-considered the clinical evidence for using bevacizumab (Avastin ®) for age related macular degeneration alongside the currently NICE approved products ranibizumab injection (Lucentis®) and aflibercept injection (Eylea®). Both Bevacizumab (Avastin®) and ranibizumab (Lucentis®) have been developed by the same pharmaceutical company. Bevacizumab is currently not licensed for use in AMD, although it has a license for use in some cancers. It is unlikely that a license for bevacizumab will be sought. Ranibizumab is a smaller molecule and was specifically developed to treat eye diseases. It is derived from the same anti-VEGF mouse monoclonal antibody as bevacizumab. Intravitreal use of bevacizumab requires much smaller doses which are produced by breaking open a vial and drawing them up into a fine syringe to deliver small volumes. The MHRA considers that this manipulation creates an unlicensed medicine as opposed to just an 'off label' medicine.

Compared with ranibizumab and aflibercept, intravitreal bevacizumab represents a substantial cost-saving for Greater Manchester.

There is now more clinical evidence available to support the use of bevacizumab in wAMD. The two-year Comparison of AMD Treatments Trials (CATT) trial in the US, which published its results in 2012, and the Inhibition of VEGF in Age-related Choroidal Neovascularisation (IVAN) trial in the UK (2013) both concluded that the two treatments (bevacizumab and ranibizumab) are equally effective. A recent Cochrane review in 2014 (which looked at the different trials to date) quashed fears that there is a greater risk of death or serious side effects using bevacizumab. The greatest risk around intravitreal use of bevacizumab appears to be from reformulation of bevacizumab into smaller volumes and the risk of infection. Infectious endophthalmitis is a medical emergency which can lead to loss of vision or even the eye itself. This risk can mostly be mitigated if supply of intravitreal bevacizumab is from a licensed supplier that undertakes the manipulation of the bevacizumab vials under aseptic conditions.

A separate cost effectiveness evaluation looking at the IVAN trial data found that the number of QALYs accrued over the 2-year trial period did not differ significantly between bevacizumab and ranibizumab, or between continuous and discontinuous treatments. Patients randomised to continuous treatment accrued *non-significantly* more QALYs than those randomised to discontinuous treatment for bevacizumab or for ranibizumab; while differences between ranibizumab and bevacizumab were negligible. This study therefore demonstrates that in the setting of the UK IVAN trial, we can be >99% confident that ranibizumab represents very poor value for money compared with bevacizumab at the £20 000 per QALY ceiling ratio used within NHS decision-making.

The acquisition cost for ranibizumab is approx £900 per dose compared to approx £75-100 per dose of bevacizumab for the manufactured intravitreal product.

Recommendation

GMMMG agreed that intravitreal bevacizumab is clinically equivalent to ranibizumab in the treatment of wet-AMD and can see the cost advantages of offering bevacizumab as an option for treatment.

However, due to national recommendations around the use of unlicensed medicinal products (the MHRA Guidance for the supply of unlicensed medicinal products and GMC guidance) GMMMG cannot recommend the commissioning of an unlicensed product for any ophthalmological condition where there is a licensed alternative. This is in line with the advice received from the Department of Health and Ministers.

This recommendation is advisory and the decision to offer bevacizumab as a treatment option will however lie with individual CCGs and be based on local priorities.

References

1. **Use of bevacizumab for wAMD document produced by RDTC® November 2015.**

Further references available on request.