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NHS Wiltshire regards eye disease and chronic long term conditions as an important area for commissioning and therefore values innovative interventions for the disease which are proven to be safe, cost effective and affordable in their implementation. We welcome the opportunity to comment on the DSU report relating to consideration of bevacizumab as a comparator in the appraisal of ranibizumab for the treatment of macular oedema caused by retinal vein occlusion.

Evidence relating to pharmaceutical quality of reformed bevacizumab as used in eye conditions

Intravitreal injections require much smaller doses of bevacizumab than those supplied for its routine licenced use as an anti-cancer drug. The use of IVB therefore adds an additional step into the preparation process which could lead to greater risk of contamination. The review reports a number of outbreaks of endophthalmitis associated with use of IVB. However the precise level of risk to patients associated with the reformed product is not clear.

Current use of Intravitreal Bevacizumab (IVB) used in the UK?

The MHRA considers that the manipulation of bevacizumab as currently required for intravitreal use creates an unlicensed product. Given the MHRA's position we would be interested in their position on its consideration as a comparator for ranibizumab a the findings of such an analysis may have significant implications for the use of an unlicensed product within the NHS.

The report concludes that in general it appears that there is already substantial use of IVB across the UK NHS but that there is substantial variation in practice. This conclusion is based on a limited number of published commissioning policies and a survey of hospital based consultant opthalmologists with a low (17%) response rate. Based on the information presented it is difficult to draw any firm conclusions on current practice and our ability to

comment on the report's conclusion is limited by the suppression of figures for the manufacture and supply of IVB.

Evidence of efficacy of IVB in adults with RVO and DMO
The evidence synthesised within the review on the efficacy of IVB is generally favourable to the use of IVB as a comparator for ranibizumab. However a number of the studies reported were of small sample size and a number of studies were only available as abstracts. No studies were presented directly comparing treatment with bevacizumab and ranibizumab. The evidence review also highlights the current lack of clarity over the most effective treatment dose and staging regime for the use of IVB in both conditions. Greater clarity over effective treatment dosages and regimes would be beneficial before proceeding with a comparator appraisal.

Adverse events from IVB in eye conditions
The analysis of adverse events presented focussed on 'important and serious adverse events' and considers treatments for a range of eye conditions. This extends the pool of studies available for consideration but potentially limits the applicability of the findings. When the results of the CATT and IVAN trials were combined there was a statistically significantly higher rate of serious systemic adverse events in the IVB group, though there were a number of potentially confounding factors reported between the treatment arms within the CATT trial which may account for this. Further information on the safety profile of IVB is needed and we would support further investigation including follow up of these studies and the analysis of wider information available from the Yellow Card Scheme and other sources.

Yours sincerely

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