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## Management of neovascular age-related macular degeneration: systematic drug class review and economic evaluation

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### Authors' objectives

The objective of this report is to assess the impact of the pharmaceutical management of neovascular age-related macular degeneration by answering the following research questions:

- What is the clinical evidence on the relative effectiveness of pegaptanib, bevacizumab, ranibizumab, triamcinolone, anecortave acetate, or placebo (either alone or in combination) versus V-PDT in neovascular AMD?
- What is the relative cost-effectiveness of the various forms of pharmaceutical management of neovascular AMD?
- What is the evidence regarding the timing for the initiation of therapy for the comparisons listed above?
- What is the evidence regarding re-treatment with a different regimen in persons who did not have satisfactory clinical response to a particular regimen?

### Authors' conclusions

The review of clinical evidence found that, with the exception of trials comparing ranibizumab with V-PDT, there was a significant lack of trials comparing the other anti-VEGF agents in general. There is only one RCT that looked at the efficacy and safety of anecortave acetate compared with V-PDT. However, although results have shown seemingly effective visual acuity improvement with bevacizumab, this was based only on three poor quality RCTs. Whether generalizations from ranibizumab to bevacizumab can be made is not clear from the evidence identified.

Six non-RCT studies suggest the combination therapies analyzed are effective. These combination therapies are typically a combination of V-PDT and anti-VEGF therapies. However, inferences regarding relative efficacy cannot be made from these study designs. Conclusions drawn by these studies need to be confirmed by results of future larger-scale randomized controlled trials.

Overall, the efficacy of anti-VEGF therapies over V-PDT is well supported by RCTs. What remains unclear is whether combination therapy (and which combinations) are superior or merely equal to monotherapy. Furthermore the efficacy of one anti-VEGF agent compared with another is also unclear and this has very important practical and economic implications. The scant nature of the evidence does not allow us to draw conclusions regarding optimal timing of initiation of therapy and re-treatment.

Between V-PDT, pegaptanib, and ranibizumab, only ranibizumab demonstrated a reversal of the degenerative process for neovascular CNV, on average. The primary economic evaluation found that the premium for using ranibizumab would not be considered cost-effective using a willingness-to-pay threshold of \$50,000. A 3.5% reduction in the price of ranibizumab would be required to achieve that. Alternately, this might be achieved by reducing the frequency of treatment below that used in the clinical trials. However evidence for the impact this might have on effectiveness is lacking. Using bevacizumab as a substitute for ranibizumab could be more effective and less costly than either VPDT or pegaptanib. However, currently there is limited clinical trial evidence on the efficacy and safety of bevacizumab in the treatment of AMD.

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