

**Macugen® (Pegaptanib sodium)**

**SUBMISSION TO THE NATIONAL INSTITUTE FOR  
HEALTH AND CLINICAL EXCELLENCE**

**31<sup>st</sup> July 2006**

## **EXECUTIVE SUMMARY**

### **Background**

- Subfoveal neovascular age-related macular degeneration (ARMD) is a progressive degenerative disease of the central retina that results in irreversible loss of central visual acuity (VA) and can rapidly lead to impaired vision and blindness.
- ARMD is the primary cause of vision loss in the Western world for people over 50 years. There are approximately 26,000 new cases of neovascular ARMD in the UK each year.
- Neovascular ARMD is associated with a high burden for patients. Decreased VA is associated with loss of independence, an increased risk of depression, falls and fractures and a decreased health-related quality of life. Patients require active treatment of their disease in order to minimise their visual loss and maintain quality of life.
- For the vast majority of people with subfoveal neovascular ARMD there are currently no active treatments available and usual care consists of visual aids and visual rehabilitation.
- Pegaptanib sodium (pegaptanib) targets the underlying pathologic process common to all subtypes of neovascular ARMD and is the only pharmacological intervention licensed for the treatment of all patients with neovascular ARMD.
- Pegaptanib is a selective vascular endothelial growth factor (VEGF) inhibitor. It is a novel, first in class treatment that specifically targets VEGF 165. Selective inhibition of VEGF 165 suppresses pathological neovascularisation, whereas pan-VEGF inhibition also affects normal compensatory revascularisation.
- Pegaptanib provides an important treatment option to a broad population of subfoveal neovascular ARMD patients where there is a high unmet need for an active treatment. The licensed dose of pegaptanib is 0.3 mg administered by intravitreal injection once every 6 weeks.

### **Clinical Effectiveness of Pegaptanib in Neovascular ARMD**

- The efficacy, safety and tolerability of pegaptanib have been studied in two identical, randomised, controlled, double-masked studies, known together as the VISION study. This study enrolled 1,208 individuals with subfoveal neovascular ARMD and compared pegaptanib with usual care.
- A broad population of individuals with a wide range of lesion subtypes were enrolled. Many enrolled patients had poor VA, large lesion size, and aggressive lesions with up to 6 disc areas of haemorrhage as well as more chronic lesions with up to 25% scarring and atrophy.
- Pegaptanib is significantly more effective than usual care in preserving VA. Following one year of treatment 70% of individuals receiving pegaptanib 0.3 mg lost less than 3 lines (15 letters) compared with 55% of individuals receiving usual care ( $p < 0.001$ ). Statistically significant benefits in VA (as measured by the mean loss in VA from baseline) with pegaptanib compared with usual care were seen as early as 6 weeks after beginning treatment.

- Pegaptanib has a sustained treatment benefit. Continued treatment with pegaptanib 0.3 mg for up to two years was significantly better than discontinuation after one year of treatment (16% vs. 27% had at least 15 letters loss, respectively).
- Treatment with pegaptanib slows progression to legal blindness. In the VISION study, compared to patients who received usual care, 36% fewer patients treated with pegaptanib 0.3 mg progressed to legal blindness over 2 years ( $p < 0.01$ ).
- In line with its targeted mechanism of action, pegaptanib demonstrates consistent efficacy in preserving vision across a broad range of subfoveal neovascular ARMD patients. Pegaptanib is effective in all patients regardless of lesion subtype, lesion size, or baseline VA when compared to usual care.
- The novel re-randomisation design used in the VISION study provides empirical evidence of a disease modifying effect for pegaptanib.
- Pegaptanib is a well tolerated treatment. Only 1% of individuals treated with pegaptanib 0.3 mg withdrew from the study due to adverse events after Year 1 and 4% after Years 1&2 of study treatment.
- The incidence of systemic adverse events with pegaptanib 0.3 mg was low and similar to that seen with usual care. Pegaptanib was not associated with systemic or non-ocular spontaneous bleeding.
- Intravitreal pegaptanib was not associated with the potential VEGF-inhibition-related adverse events recognised with systemic administration of non-selective pan-VEGF inhibitor agents; such as hypertension, thromboembolic events or serious haemorrhagic events.
- Patient compliance was high. Over the 2-year period, 92% of injections occurred within one week of the scheduled dose of both pegaptanib 0.3 mg and usual care.

### **Cost Effectiveness of Pegaptanib versus Usual Care in Neovascular ARMD**

- A cost-utility analysis is presented estimating the incremental cost per quality adjusted life year gained (IC/QALY) for patients treated with pegaptanib 0.3 mg versus usual care. The approach adopted is analogous to that reported by NICE, in 2003, for the cost-effectiveness of photodynamic therapy (PDT).
- Usual care was defined as best supportive care, i.e. minimal use of PDT with verteporfin for patients with predominantly classic lesions, and provision of support services for patients with a VA of 6/60 or below. This analysis was performed specifically for England and Wales; the cost year was 2005.
- A targeted treatment approach is modelled where pegaptanib is administered every 6 weeks but discontinued in patients whose vision falls below specified clinical thresholds. A maximum of two years of treatment is presented.
- Cost-effectiveness was modelled over 10 years. Extrapolation of pegaptanib's benefit on a patient's vision after discontinuation is supported from empirical evidence of pegaptanib's disease modifying effect.
- The base case analysis (Scenario A) assumed that patients with a best-corrected VA in their better-seeing eye of 6/12 to 6/95 (inclusive) receive a maximum of 2 years of treatment. Treatment was terminated at any time if individual patients' VA dropped below 6/95, and at 1 year if they had experienced severe vision loss (loss of 6 or more lines from the pre-treatment level). An alternative case (Scenario B) included patients with a best-corrected

VA in their better-seeing eye of 6/12 to 6/60, with treatment terminated when VA dropped below 6/60.

- Resource use estimates for the administration of the treatment regimens and management of adverse events were developed by structured interview of three consultant ophthalmologists. Other model parameters were obtained from the published literature. Unit costs were obtained from national sources.
- The IC/QALY was estimated as £15,815 for the base case (Scenario A). The probability of cost-effectiveness at a threshold of £20,000/QALY was 78% and at £30,000/QALY was 99%. For the alternative case (Scenario B) the IC/QALY was estimated as £14,202. The probability of cost-effectiveness at a threshold of £20,000/QALY was 86% and at £30,000/QALY was 99%.
- The IC/QALY estimate remained below a threshold of £30,000 in all sensitivity analyses with the exception of analysis time frames of 5 years or less for the base case (Scenario A) and 4 years or less for the alternative case (Scenario B). Furthermore, the IC/QALY estimate was less than £20,000 in all sub-populations investigated, including patients with predominantly classic, minimally classic, and occult lesion types, and in large as well as small lesions.
- Pegaptanib 0.3 mg is expected to be cost-effective in all patient groups and provides an important treatment option to a broad population of subfoveal neovascular ARMD patients.

#### **Wider Implications to the NHS with Pegaptanib in Neovascular ARMD**

- The number of patients expected to receive pegaptanib for the base case if patients with a VA of 6/12 to 6/95 (inclusive) are treated (Scenario A) is estimated to be 234 in 2006, rising to 2,747 in 2010. With the alternative case where the VA range is limited to 6/12 to 6/60 (Scenario B), these estimates are reduced to 212 in 2006 and 2,490 in 2010.
- The direct cost associated with pegaptanib treatment for a period of up to 2 years is estimated as approximately £1.2 million in 2006 for the base case (Scenario A) or £1.1 million for the alternative case (Scenario B). The direct cost is estimated to rise to a total of £22.4 million in 2010 for the base case (Scenario A) or £19.1 million for the alternative case (Scenario B).
- Direct cost savings associated with pegaptanib use are expected to result from improved visual outcomes, including savings to the NHS and PSS associated with blind registration, low vision aids, rehabilitation, community and residential care.
- Cost savings are estimated to total £101,000 in 2006, rising to £3.8 million in 2010 for the base case (Scenario A) or £98,000 rising to £3.7 million for the alternative case (Scenario B). Due to the disease modifying effect of pegaptanib, further cost savings would be realised beyond 2010. For a 10 year follow-up, cost savings estimated to total an additional £18.3 million for the base case (Scenario A) and £16.6 million for the alternative case (Scenario B) could be realised between 2011 and 2015.
- The introduction of pegaptanib in England and Wales is associated with a net direct cost estimated as approximately £1.1 million in 2006 increasing to £18.5 million in 2010 for the base case (Scenario A) or £1.0 million increasing to £15.4 million for the alternative case (Scenario B)

- Pegaptanib represents a valuable treatment option for subfoveal neovascular ARMD patients in England and Wales, who have an unmet need for an active treatment.

Declaration

This submission contains all the relevant evidence in the possession of Pfizer Limited related to the clinical and cost-effectiveness appraisal of Pegaptanib sodium.

**Signed:**      **Position**

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Acting Team Leader OR&EBM
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