NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Pegaptanib sodium for the treatment of diabetic macular oedema

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pegaptanib sodium within its licensed indication for the treatment of diabetic macular oedema.

Background

The macula is the central part of the retina responsible for colour vision and perception of fine detail. Diabetic macular oedema (DMO) is the main cause of visual loss in diabetic maculopathy, a type of diabetic eye disease which involves localised damage to the macula. DMO occurs as a result of changes in retinal blood vessels in people with diabetes. A reduction in the number of connective tissues around capillaries and an increased amount of vascular endothelial growth factor (VEGF) causes increased permeability of the blood-retinal barrier. This leads to leakage of plasma constituents in the surrounding retina, causing oedema which disrupts the fovea, the area responsible for sharp vision. It can lead to severe visual impairment in the affected eye.

Diabetic maculopathy can be classified as focal, diffuse, ischaemic or mixed, depending on the location of leakage or loss of blood supply due to capillary loss. Focal maculopathy is localised leakage of tissue fluid from tiny swellings in the wall of retinal capillaries. Diffuse maculopathy refers to generalised thickening of the central macula caused by widespread leakage from dilated capillaries. Ischaemic maculopathy occurs when the blood vessels in the macula become constricted and starve the macula of oxygen and nutrition, and is associated with a significant risk to vision. Mixed maculopathy refers to cases with a combined pathology, particularly of diffuse oedema and ischaemia.

The majority of visual loss occurs when DMO involves the centre of the macula. This is known as clinically significant macular oedema and is regarded as the threshold level for treatment. Clinically significant macular oedema occurs if there is thickening of the retina involving the centre of the macula and if there are hard exudates.

In 2009, 2.4 million people were diagnosed with diabetes in England and Wales. Approximately 14% of people with diabetes have DMO and the prevalence increases to 29% for people with diabetes who use insulin for more than 20 years. Approximately 6% of people with diabetes have clinically significant macular oedema. When DMO is untreated there is a 25-30% risk of developing clinically significant macular oedema. Moderate visual loss will occur in approximately 24% of untreated eyes where clinically significant

macular oedema has developed. In addition to duration of diabetes, risk factors include older age, poor glucose control, high blood pressure, nephropathy (kidney disease), pregnancy, smoking, obesity and having a high cholesterol level. Diabetes is more common in African-Caribbean and South Asian people.

Treatment of systemic risk factors, including dietary intake and blood pressure control, may delay disease progression. Laser therapy (photocoagulation) is the main treatment option for sight-threatening focal, diffuse or mixed DMO. The aim of photocoagulation is to prevent further visual loss. Focal laser treatment is used to treat focal DMO and grid laser treatment is used to treat diffuse DMO. Severe diffuse macular oedema which is non-responsive to grid laser photocoagulation may be treated with surgery. Visual loss with ischaemic maculopathy cannot be treated. Currently there are no licensed pharmacological agents to treat DMO. In some clinical centres in the NHS, bevacizumab is used outside its licensed indication where photocoagulation has failed to produce a response or as an alternative treatment option where long term treatment with photocoagulation is considered a risk. NICE is currently appraising ranibizumab for the treatment of DMO.

The technology

Pegaptanib sodium (Macugen, Pfizer) is a selective VEGF inhibitor. Pegaptanib binds to extracellular VEGF thereby inhibiting the growth of new blood vessels. It is administered by intravitreal injection.

Pegaptanib sodium does not currently have a UK marketing authorisation for the treatment of DMO. It has been studied in clinical trials in people with DMO as a monotherapy compared with sham injection. Some of the trials specified inclusion of people with DMO involving the centre of the macula.

Intervention(s)	Pegaptanib sodium
Population(s)	Adults with diabetic macular oedema
Comparators	• Laser photocoagulation including grid laser and focal laser photocoagulation • Ranibizumab (subject to NICE appraisal) • Bevacizumab
Outcomes	The outcome measures to be considered include: • Best corrected visual acuity (the affected eye) • Best corrected visual acuity (both eyes) • Intraocular pressure

	• Cataracts • Mortality • Stroke • Adverse effects of treatment • Health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	If the evidence allows, consideration will be given to subgroups according to: • type of DMO (focal, diffuse or centre-involving); • baseline visual acuity; • number of previous treatments with laser photocoagulation. Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal in Preparation, 'Ranibizumab for the treatment of macular oedema caused by retinal vein occlusion'. Earliest date of publication TBC Technology Appraisal in Preparation, 'Dexamethasone intravitreal implant for the treatment of macular oedema caused by retinal vein occlusion'. Earliest date of publication TBC. Technology Appraisal in Preparation, 'Ranibizumab for the treatment of diabetic macular oedema'. Earliest date of publication TBC Proposed Technology Appraisal, 'Fluocinolone acetonide intravitreal insert for the treatment of diabetic macular oedema'. Related Guidelines: Clinical Guideline No.66, May 2008, 'Type 2 diabetes:

	the management of type 2 diabetes'. Related Interventional Procedures: Interventional Procedure No. 72, Jul 2004, 'Arteriovenous crossing sheathotomy for branch retinal vein occlusion'.

Questions for consultation

Have the most appropriate comparators for the treatment of diabetic macular oedema been included in the scope? Are the comparators listed routinely used in clinical practice?

- Should fluocinolone acetonide intravitreal implant be included as a comparator?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising pegaptanib sodium through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)