Evidence Review for Prescribing Clinical Network

Treatment: Ranibizumab (Lucentis®) for treating choroidal neovascularisation associated with pathological myopia

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Summary page

- How strong is the evidence for claimed efficacy?
  (Grade A = > 1 RCT or meta-analysis; Grade B = 1 RCT or descriptive study; Grade C = expert committee report/opinion)

A

- Potential advantages in terms of: efficacy, compliance, pharmacokinetics, drug interactions and adverse effects?

Only drug with a NICE TA for choroidal neovascularisation

- Is there a clear place in therapy / treatment pathway?
  (E.g. patient type / characteristics, and relationship to other therapies)

Yes

- Is monitoring for toxicity required?

Yes

- Is dose titration required?

No

- Traffic light status (ie who will prescribe the drug and any restrictions required)?

Red

- Role of the specialist (if applicable)?

Administration and monitoring

- Role of GP (if applicable)?

Nil

- Financial implications?

This will be an added cost to the CCG

- Other issues

Nil

- National Guidance available

NICE TA

Recommendations:

As a NICE technology appraisal CCG's will need to make ranibizumab available for treating choroidal neovascularisation associated with pathological myopia in line with the NICE recommendations. This should remain a hospital only RED drug.

VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
1	16/12/2013	Lucy Alexakis		

1. Purpose of the Review

NICE TA 298 Ranibizumab for treating choroidal neovascularisation with pathological myopia was published November 2013. The purpose of this review is to implement NICE (1).

The purpose of this review is not to replicate the work already done by NICE.

2. Appropriateness

2.1 The patient and 2.2 The problem:

Patients with visual impairment due to choroidal neovascularisation secondary to pathological myopia.

Definition:

Choroidal neovascularization (CNV) involves the growth of new blood vessels that originate from the choroid through a break in the Bruch membrane into the sub–retinal pigment epithelium (sub-RPE) or subretinal space. CNV is a major cause of visual loss.

2.3 The Intervention:

Ranibizumab (Lucentis®) intravitreal injection

How does it work:

Ranibizumab is a humanised recombinant monoclonal antibody fragment targeted against human vascular endothelial growth factor A (VEGF-A). It binds with high affinity to the VEGF-A isoforms (e.g. $VEGF_{110}$, $VEGF_{121}$ and $VEGF_{165}$), thereby preventing binding of VEGF-A to its receptors VEGFR-1 and VEGFR-2. Binding of VEGF-A to its receptors leads to endothelial cell proliferation and neovascularisation, as well as vascular leakage (2).

Care setting: Secondary care, administration by a consultant ophthalmologist.

Frequency: Treatment is initiated with a single injection.

If monitoring reveals signs of disease activity, e.g. reduced visual acuity and/or signs of lesion activity, further treatment is recommended.

Monitoring for disease activity may include clinical examination, optical coherence tomography (OCT) or fluorescein angiography (FA).

While many patients may only need one or two injections during the first year, some patients may need more frequent treatment. Therefore, monitoring is recommended monthly for the first two months and at least every three months thereafter during the first year. After the first year, the frequency of monitoring should be determined by the treating physician.

The interval between two doses should not be shorter than one month (2).

2.4 Alternative treatments:
There are currently no treatments commissioned for choroidal neovascularisation associated with pathological myopia in Surrey CCG's, Crawley CCG, Horsham and Mid Sussex CCG. Funding would be via an Individual Funding Request.

- Photodynamic therapy (Verteporfin), however this is not effective in most patients and its use is diminishing because of anti-VEGF treatments.
- Bevacizumab is an alternative anti VEGF however is unlicensed for all ophthalmology indications
- Aflibercept is an alternative anti VEGF however is not licensed for choroidal neovascularisation

3. Effectiveness

3.1 Expected benefits
Gain in visual acuity and visual function. Prevention of blindness.

3.2 Is there a plausible biological basis for effectiveness?
Yes, by preventing binding of VEGF-A to its receptors will lead to reduced neovascularisation.

3.3 Side-effects/complications
The majority of adverse reactions reported following administration of Lucentis are related to the intravitreal injection procedure.

The most frequently reported ocular adverse reactions following injection of Lucentis are: eye pain, ocular hyperaemia, increased intraocular pressure, vitritis, vitreous detachment, retinal haemorrhage, visual disturbance, vitreous floaters, conjunctival haemorrhage, eye irritation, foreign body sensation in eyes, increased lacrimation, blepharitis, dry eye and eye pruritus.

The most frequently reported non-ocular adverse reactions are headache, nasopharyngitis and arthralgia.

Less frequently reported, but more serious, adverse reactions include endophthalmitis, blindness, retinal detachment, retinal tear and iatrogenic traumatic cataract (2)

3.4 Review of evidence (See Appendix 1. for Search Strategy and Summary of Results)

NICE Guidelines
NICE TA 298 Ranibizumab for treating choroidal neovascularisation associated with pathological myopia. November 2013.
Ranibizumab is recommended as an option for treating visual impairment due to chorodial neovascularisation secondary to pathological myopia when the manufacturer provides ranibizumab with the discount agreed in the patient access scheme.

SMC Guidance

The SMC has accepted ranibizumab for treatment for visual impairment due to choroidal neovascularisation secondary to pathologic myopia in adults.

4. Summary of Key Points for Consideration

4.1 National guidance

NICE TA 298 Ranibizumab is recommended as an option for treating visual impairment due to choroidal neovascularisation secondary to pathological myopia when the manufacturer provides ranibizumab with the discount agreed in the patient access scheme (1).

4.2 Efficacy

Ranibizumab was compared against verteporfin photodynamic therapy (v PDT), in the RADIANCE trial which was reviewed by NICE. The trial showed that ranibizumab was associated with greater improvement than (v PDT) in best corrected visual acuity between baseline and months 1-3. There is uncertainty about the efficacy after 3 months.

4.3 Potential Benefits over existing therapy

- Greater improvement in best corrected visual acuity compared to verteporfin photodynamic therapy

4.4 Potential disadvantages

- This is an increased cost to the CCG, however number of injections per year are likely to be only 1 or 2 injections

4.5 Budgetary Impact

4.5.1 Cost:

Ranibizumab 10mg/ml list price is £742.17.

There is a patient access scheme in place for ranibizumab, however this is commercially sensitive and cannot be printed in this document.

Treatment is commenced with a single injection, monitoring will determine if further injections are required.

5. Conclusions and Recommendations

To be commissioned as a hospital only RED drug in line with NICE TA 298, as an option for treating visual impairment due to choroidal neovascularisation secondary to pathological myopia.

Appendix 1: Evidence search

Search terms used: Ranibizumab, Choroidal neovascularisation, pathological myopia

Resource	Used in this review?
National Library for Health (NHL) http://www.library.nhs.uk/Default.aspx A gateway site with access to other resources such as Reviews (Bandolier, Cochrane, CRD etc), Guidelines (e.g. NICE), Clinical Knowledge Summaries (CKS) and Journals including AMED, British Nursing Index, CINAHL, E-books, EMBASE, HMIC, MEDLINE, My Journals, PsycINFO, PubMed, Databases from Dialog.	✓
National Institute of Health and Clinical Excellence (NICE) http://www.nice.org.uk/ NICE produces national guidance in three areas of health: 1. Public health - guidance on the promotion of good health and the prevention of ill health 2. Health technologies - guidance on the use of new and existing medicines, treatments and procedures within the NHS 3. Clinical practice - guidance on the appropriate treatment and care of people with specific diseases and conditions within the NHS.	✓ (through NHL)
Bandolier http://www.medicine.ox.ac.uk/bandolier/index.html Bandolier is a website about the use of evidence in health, healthcare, and medicine. Information comes from systematic reviews, meta-analyses, randomised trials, and from high quality observational studies.	✓(through NHL)
Centre for Reviews and Dissemination http://www.york.ac.uk/inst/crd/ CRD undertakes high quality systematic reviews that evaluate the effects of health and social care interventions and the delivery and organisation of health care. Databases maintained by CRD include Database of Abstracts of Reviews of Effects (DARE), NHS Economic Evaluation Database (NHS EED), Health Technology Assessment (HTA) Database	✓(through NHL)
Scottish Intercollegiate Guidelines Network (SIGN) http://www.sign.ac.uk/ Scottish equivalent of NICE	✓
Medical Services Advisory Committee (Australia) http://www.msac.gov.au/internet/msac/publishing.nsf/Content/home-	✓

1 The principal role of the Medical Services Advisory Committee (MSAC) is to advise the Australian Minister for Health and Ageing on evidence relating to the safety, effectiveness and cost-effectiveness of new medical technologies and procedures.	
Canadian Agency for Drugs and Technologies in Health (CADTH) http://www.cadth.ca/index.php/en/home The Canadian Agency for Drugs and Technologies in Health (CADTH) is a national body that provides Canada's federal, provincial and territorial health care decision makers with credible, impartial advice and evidence-based information about the effectiveness and efficiency of drugs and other health technologies.	✓

Appendix 2: Grading of evidence

- Ia: systematic review or meta-analysis of randomised controlled trials
- Ib: at least one randomised controlled trial
- IIa: at least one well-designed controlled study without randomisation
- IIb: at least one well-designed quasi-experimental study, such as a cohort study
- III: well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, case–control studies and case series
- IV: expert committee reports, opinions and/or clinical experience of respected authorities

Appendix 3: References

1. www.nice.org.uk. TA298. Ranibizumab for treating choroidal neovascularisation associated with pathological myopia. November 2013.
2. www.medicines.org.uk . Ranibizumab (Lucentis ®). Last updated 17/7/2013. Accessed 16/12/2013.