Item Number: 10

Name of Presenter: Andrew Phillips

Meeting of the Governing Body

4 December 2014

NHS
Vale of York
Clinical Commissioning Group

Commissioning an Alternative Anti-VEGF Service

Purpose of Report
For Approval

1. Rationale

To gain approval for the development of a business case for the provision of a Bevacizumab only service for Age Related Macular Degeneration

2. Strategic Initiative

- ☐ Integration of care
- ☐ Person centred care
- ☐ Primary care reform
- ☐ Urgent care reform
- ☒ Planned care
- ☐ Transforming MH and LD services
- ☐ Children and maternity
- ☐ Cancer, palliative care and end of life care
- ☐ System resilience

3. Actions / Recommendations

The Governing Body is asked to:

- Acknowledge the opportunity cost of continuing with the current commissioning policy for Anti-VEGF agents.
- Approve the preparation of a business case for the provision of this service with a commencement date of 1 April 2015.
- Agree that an open letter be issued, either alone or with other CCGs, to the General Medical Council calling for a change in the guidance around the prescribing of “unlicensed medicines” in order to allow clinicians to comply with paragraph 18 of Good Medical Practice which states “You must make good use of the resources available to you”.

4. Engagement with groups or committees

Discussions ongoing with local patient groups.

5. Significant issues for consideration

The key issue is the effective deployment of CCG resources for the protection of the eyesight of local people.

6. Implementation

The innovation, finance and contracting teams will need to prepare the business case under the leadership of Michael Ash-McMahon

7. Monitoring

The Governing Body should expect to receive the final business case at the February 2015 meeting for sign off.

8. Responsible Chief Officer and Title Michael Ash-McMahon Interim Chief Finance Officer	**9. Report Author and Title** Michael Ash-McMahon
10. Annexes Not applicable	

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Commissioning an Alternative Anti-VEGF Service

1. Background

1.1 Bevacizumab (pronounced bev-a-Sizz-uh-mab), trade name Avastin, is a recombinant humanized monoclonal antibody that blocks angiogenesis (new blood vessel growth) by inhibiting vascular endothelial growth factor A (VEGF-A). VEGF-A is a chemical signal that stimulates angiogenesis in a variety of diseases, including Age Related Macular Degeneration (ARMD).

1.2 The American Macular Degeneration Foundation[1] reported in 2005, "*Early study results indicate that a potential new age-related macular degeneration (AMD) therapy may improve vision within one week of injection …… Researchers at the University of Miami's Bascom Palmer Eye Institute said Avastin (bevacizumab) substantially reduced blood vessel leakage contributing to vision loss…..The use of Avastin (bevacizumab) for macular degeneration is "off label."*

1.3 Bevacizumab was created by Genetech as a treatment for bowel and breast cancer and it is licensed for these conditions. Following the initial results of using it in the treatment ARMD Genetech created a second, related, product ranibizumab (Lucentis) from the same parent mouse antibody. The Genetech Company subsequently became a subsidiary of Roche in 2009. When it came to marketing ranibizumab, Roche decided to do this jointly with Novartis by giving them responsibility for sales in Europe.

1.4 In 2008 ranibizumab was approved by NICE to be used in the treatment of ARMD but it was controversial from the start as the price was set significantly higher than that of bevacizumab.

1.5 Following the arrival of this licensed product clinicians were placed in a situation whereby they were obliged by the guidance of the General Medical Council (GMC) [2] to stop using bevacizumab. See para 68 "Good practice in Prescribing and managing medicines and devices".

68. You should usually prescribe licensed medicines in accordance with the terms of their licence. However, you may prescribe unlicensed medicines where, on the basis of an assessment of the individual patient, you conclude, for medical reasons, that it is necessary to do so to meet the specific needs of the patient.

1.6 It is unlikely that bevacizumab will ever be given a license for use in the eye as the only body that can seek a license is the manufacturer which in the case of both bevacizumab and ranibizumab is Genetech.

1.7 In December 2011 the Royal College of Ophthalmologists (RCOphth) published the results of a working group of experts [3] and concluded that *"both are equally effective in the treatment of AMD and have a similar safety profile……. The use of Avastin instead of Lucentis would save the NHS considerable sums of money but when Avastin is used for the treatment of eye disease it is used "off-label". Current General Medical Council (GMC) guidance states that doctors who prescribe off-label must be satisfied that doing so would better serve the patient's needs than using an appropriately licensed alternative. There is no evidence that Avastin is more effective than Lucentis for the treatment of AMD."*

1.8 On the basis of this GMC guidance the RCOphth *declared "The College supports the continued use of Lucentis rather than Avastin for patients with wet AMD who fall within the National Institute for Health and Clinical Excellence (NICE) guidelines for treatment. The College believes that the NHS executive should urgently instruct NICE and the Medicines and Healthcare Products Regulatory Agency (MHRA) to evaluate the use of Avastin in the treatment of AMD and produce National Guidelines for the use of anti-VEGF agents in AMD."*

1.9 The pricing anomaly and subsequent opportunity cost for society inspired clinicians in the USA and UK to undertake comparative trials of bevacizumab and ranibizumab, these trials reported their results in 2012. The **C**omparison of **A**MD **T**reatments **T**rials (**CATT**) [4] in the US and the **I**nhibit **V**EGF in **A**ge related choroidal **N**eovascularisation trial (**IVAN**) [5] in the UK, reported that the two drugs were equally efficacious but commented that the trials were not "powerful" enough to comment on safety.

1.10 In February 2014 the Italian Competition Authority [6] found Roche and Novartis guilty of "*infringing article 101 TFEU by participating in an anticompetitive agreement in the market for ophthalmic drugs used to treat ARMD. Roche and Novartis set up a complex collusive strategy, with a view to avoiding that the commercial success of Lucentis be hindered by the ophthalmic applications of Avastin".* For this behaviour they were collectively fined Euro180 million.

1.11 In April 2014 Reuters [7] reported that *"France's competition authority is investigating drug makers Roche and Novartis on suspicion they were involved in anti-competitive practices in relation to eye disease treatments…… Although Roche's Avastin is not approved as a treatment for AMD, it works in a similar way to Lucentis and costs around 30 euros a dose in France versus the 900 euros charged for an injection of Lucentis."*

1.12 In September 2014 the Cochrane Review [8] on these treatments was published which found the two drugs to be equally safe, stating *"Health policies which favour using ranibizumab for treating eye disease in older people over safety concerns for a cheaper alternative should take account of a new Cochrane Review published today…. Contrary to what was argued by*

some experts, the review has found that the cheaper drug, bevacizumab, does not appear to increase deaths or serious side effects compared with ranibizumab in people with neovascular age-related macular degeneration."

1.13 A week afterwards the British Medical Journal published a blog from David Lock [9], a barrister and QC and member of the BMA Ethics Committee, which concluded stating, *"Removing the choice from clinicians between Avastin and Lucentis for routine wet AMD cases seems to be the right policy decision to promote cost effective medical treatment for NHS patients. However, the difficult question will be how many NHS commissioners have been down the yellow brick road to collect their portion of the lion's courage and will do so."*

1.14 On 19 November 2014 the BMJ published an editorial [10] by Professor Andrew Lotery (University of Southampton) and Prof Carrie McEwen, President of the Royal College of Ophthalmologists titled *"What is stopping the NHS from using bevacizumab for macular degeneration and other retinal disorders?"* The article finished with this call to the government. "*The hospital eye service is facing a serious and ever increasing capacity problem because of the demand for frequent intravitreal injections. Consequently, patients may not be getting treatment when they need it and not getting best results. The money saved by switching to bevacizumab could facilitate investment in these services. Given the overwhelming evidence for the effectiveness and safety of bevacizumab in the treatment of neovascular AMD, central government should act to overcome the bureaucratic hurdles that prevent its use."*

2. Local Context

2.1 The leaders of the CCG began discussing the use of bevacizumab with the local ophthalmologists in 2011 when the CCG was in shadow form. As described above the hurdles of efficacy and safety have been overcome leaving only the GMC guidance on "off-label" use of medicines as an issue.

2.2 The CCG currently commissions approximately 9000 anti-VEGF injections a year and this number rises each year as the age profile of our population is getting older.

2.3 The CCG has been in contact with manufacturing unit of the Royal Liverpool and Broadgreen University Hospitals pharmacy to establish the availability of bevacizumab formulated for use in the eye. We have been assured that they would have no problem in supplying sufficient quantities of bevacizumab from April 2015.

2.4 Subject to further detailed analysis as part of the proposed business case, early calculations suggest that the CCG could save up to £4 million pounds per year by switching to bevacizumab. Nationally this could represent a saving to the NHS of approximately £800 million.

3. Opportunity Cost

3.1 *"The cost of an alternative that must be forgone in order to pursue a certain action or the benefits you could have received by taking an alternative action."*

3.2 A "no change" policy for the commissioning of ARMD and other Anti-VEGF responsive conditions would mean the continuation of a £4 million opportunity cost on the local health system. In effect we would be denying the local population £4 million of other effective treatments.

3.3 To illustrate the effect of this on the local community the list below shows a number of services that each cost £4 million.

Table 1

Service or Treatment Type	Time
Community Nursing	Almost 1 year
Community Hospitals	Over 1 year
Full A&E Department	Over 6 months
5000 Cataract Operations	n/a
8 Bed Neonatal Intensive Care Unit	1 year

4. Summary

4.1 The key considerations when making any recommendation are:

1. The available evidence tells us that bevacizumab and ranibizumab are equivalent in effectiveness and safety.
2. Bevacizumab is a safe licensed product that is used at a much higher dosage in bowel and breast cancer. The description of its use in ARMD is "off-label" and is widely used in the NHS for other conditions of the eye where there is no licensed alternative.
3. The scale of the opportunity cost associated with not using bevacizumab is such that we are obliged to explore every possible avenue to correct this on behalf of the local community.

5. Recommendation

The Governing Body is asked to:

5.1 Acknowledge the opportunity cost of continuing with the current commissioning policy for Anti-VEGF agents.

5.2 Approve the preparation of a business case to fully assess the implications of a "Bevacizumab First" commissioning policy to commence in April 2015.

5.3 Agree that an open letter be issued, either alone or with other CCGs, to the General Medical Council calling for a change in the guidance around the prescribing of "unlicensed medicines" in order to allow clinicians to comply with paragraph 18 of Good Medical Practice which states "You must make good use of the resources available to you".

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