East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG, Surrey Heath CCG, Crawley CCG, Horsham & Mid-Sussex CCG

Briefing Paper for Prescribing Clinical Network on NICE Technology Appraisals: Local implementation

NICE TA Guidance	Aflibercept for treating visual impairment caused by macular oedema after branch retinal vein occlusion Technology appraisal guidance 409		
Available at	https://www.nice.org.uk/guidance/ta409		
Date of issue	28 September 2016	**Implementation deadline**	28 December 2016

Medicine details[1]	
Name, brand name and manufacturer	Aflibercept (Eylea) Bayer plc
Licensed indication	Eylea is indicated for adults for the treatment of • visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO).
Formulation	Eylea 40 mg/ml solution for injection in a vial. Each vial contains 100 microlitres, equivalent to 4 mg aflibercept. This provides a usable amount to deliver a single dose of 50 microlitres containing 2 mg aflibercept. Aflibercept solution for injection is administered by intravitreal injection.
Usual dosage	The recommended dose for Eylea is 2 mg aflibercept equivalent to 50 microlitres. After the initial injection, treatment is given monthly. The interval between two doses should not be shorter than one month. If visual and anatomic outcomes indicate that the patient is not benefiting from continued treatment, Eylea should be discontinued. Monthly treatment continues until maximum visual acuity is achieved and/or there are no signs of disease activity. Three or more consecutive, monthly injections may be needed. Treatment may then be continued with a treat-and-extend regimen with gradually increased treatment intervals to maintain stable visual and/or anatomic outcomes, however there are insufficient data to conclude on the length of these intervals. If visual and/or anatomic outcomes deteriorate, the treatment interval should be shortened accordingly.

	The monitoring and treatment schedule should be determined by the treating physician based on the individual patient's response. Monitoring for disease activity may include clinical examination, functional testing or imaging techniques (e.g. optical coherence tomography or fluorescein angiography).

Disease and potential patient group[2]

Brief description of disease

Retinal vein occlusions (RVOs) are the second most common type of retinal vascular disorder after diabetic retinal disease. They can occur at almost any age (although typically in middle to later years - most in those aged over 65 years) and their severity ranges from asymptomatic to a painful eye with severe visual impairment.

Retinal vein occlusion is one of the most common causes of sudden painless unilateral loss of vision. Loss of vision is usually secondary to macular oedema. Occlusion may occur in the central retinal vein or branch retinal vein.

Branch retinal vein occlusion

Branch retinal vein occlusions (BRVOs) are three times more common than central retinal vein occlusions (CRVOs). There are various subclassifications of this depending on whether a major branch, a minor macular branch or a peripheral branch is affected. Each carries its own prognosis. A hemiretinal vein occlusion refers to an occlusion that is proximal enough to affect half of the retinal drainage (ie the superior or inferior portion) as opposed to the smaller portion affected by a BRVO.

Presentation

This largely depends on the amount of compromise to macular drainage. The most common presentation is of unilateral, painless blurred vision, metamorphopsia (image distortion) ± a field defect (usually altitudinal). Peripheral occlusions may be asymptomatic. Visual acuity depends on the degree of macular involvement.

Fundoscopy will reveal vascular dilatation and tortuosity of the affected vessels, with associated haemorrhages in that area only (look for an arc of haemorrhages, like a trail left behind a cartoon image of a shooting star).

Potential patient numbers per 100,000[3]

Estimated number of people who start treatment with aflibercept each year in England and local CCGs. See NICE Resource Impact Report for full assumptions.[3]

Table 1 : England

Population	Proportion of total population	Number of people
Adults aged 45 and over	100%	22,902,461
Estimated incidence: people with BRVO	0.12%	27,483
People with BRVO and macular oedema	85%	23,361
People with BRVO and macular oedema who experience visual impairment	50%	11,680

Eligible population		11,680

Table 2: Local CCGs

Population	Crawley	HMS	East Surrey	G&W	NW Surrey	Surrey Downs	Surrey Heath
Adults aged 45 and over	39,800	105,178	77,995	90,549	147,123	135,147	42,596
Estimated incidence: people with BRVO	48	126	94	109	177	162	51
People with BRVO and macular oedema	41	107	80	92	150	138	43
People with BRVO and macular oedema who experience visual impairment	20	54	40	46	75	69	22
Eligible population	**20**	**54**	**40**	**46**	**75**	**69**	**22**

SUMMARY

Guidance[4]

Recommendation:
Aflibercept is recommended as an option within its marketing authorisation for treating visual impairment in adults caused by macular oedema after branch retinal vein occlusion, only if the company provides aflibercept with the discount agreed in the patient access scheme.

Cost implications

Cost:
The list price of aflibercept is £816 for 1 vial (excluding VAT; British National Formulary, accessed May 2016).

Annual cost per patient:
There are patient access schemes for both ranibizumab and aflibercept where the level of discount is commercial in confidence.

Based on the list price:
1 year of aflibercept = £816 x 12 = £9792

Availability of PAS and details (if appropriate):
The company has agreed a patient access scheme with the Department of Health.

This scheme provides a simple discount to the list price of aflibercept, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence.

The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS.

Availability of homecare service (if appropriate):
Not appropriate.

Alternative treatments and cost per patient per year

Other NICE recommended products:
Based on the list price:

1 year of aflibercept = £816 x 12 = £9,792
1 year of ranibizumab = £742 x 12 = £8,904
1 year of dexamethasone intravitreal implant = £870 x 3 = £2,610

Options not reviewed by NICE but used in standard practice:

Impact to patients

- Patients would welcome additional options to treat visual impairment caused by macular oedema after branch retinal vein occlusion.

Impact to primary care prescribers

- This is a PbRe drug and is commissioned by CCGs for use in secondary care. There should be no prescribing in primary care.
- Primary care prescribers should be aware that their patient is receiving aflibercept in order to be alert to potential side-effects and interactions with other medicines prescribed in primary care.

Impact to secondary care

- The initiation, administration and on-going treatment is managed by secondary care.
- Prescribers would welcome additional options to treat visual impairment caused by macular oedema after branch retinal vein occlusion.

Impact to CCGs

- The technology is commissioned by clinical commissioning groups (CCGs).
- Providers are NHS hospital trusts.

Implementation

- NICE TA implementation must be within 90 days of publication – 28 December 2016
- Blueteq forms to be developed
- Pathway to be discussed at Ophthalmology Network to consider:
    - Since NICE published guidance its technology appraisal on ranibizumab and dexamethasone, clinical practice has changed and anti-VEGF and corticosteroid treatments are used in the initial treatment of visual impairment caused by macular oedema after branch retinal vein occlusion
    - NICE concluded that on the basis of the trial evidence, aflibercept is more clinically effective than laser photocoagulation for untreated visual impairment caused by macular oedema after branch retinal vein occlusion and clinical experience suggests that aflibercept is more clinically effective when given before, rather than after, laser photocoagulation
    - NICE also concluded that aflibercept is more effective than dexamethasone and equivalent to ranibizumab in terms of clinical effectiveness
    - This TA allows for the use of aflibercept without the prior use of laser photocoagulation if appropriate. NICE TA283 recommends the use of ranibizumab following branch retinal vein occlusion *only if treatment with laser*

photocoagulation has not been beneficial, or when laser photocoagulation is not suitable because of the extent of macular haemorrhage

- Stopping criteria is as per The Royal College of Ophthalmologists - Retinal Vein Occlusion (RVO) Guidelines July 2015:
  Stopping ranibizumab and aflibercept therapy should be considered if after three consecutive monthly treatments, visual acuity has not improved by at least five letters and CMT has not reduced from baseline. However, reduction in retinal oedema without VA improvement or deterioration (i.e. stable VA) may be accepted as a favourable, but suboptimal outcome. Stopping ranibizumab and aflibercept therapy is recommended if after six consecutive monthly treatments, visual acuity has not improved by at least five letters and CMT has not reduced from baseline

Recommendation to PCN

PbRe:
Yes

Recommended traffic light status:
Red

Additional comments:

References:

1 Specification of Product Characteristics. Eylea 40mg/ml solution for injection in a vial. Available at: https://www.medicines.org.uk/emc/medicine/272242

2 Patient. Available at: http://patient.info/doctor/retinal-vein-occlusions

3 NICE Resource impact report: Aflibercept for treating visual impairment caused by macular oedema after branch retinal vein occlusion. Published 28 September 2016. Available at: https://www.nice.org.uk/guidance/ta409/resources

4 NICE Technology appraisal 409: Aflibercept for treating visual impairment caused by macular oedema after branch retinal vein occlusion. Published 28 September 2016. Available at: https://www.nice.org.uk/guidance/ta409

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Declaration of Interest:

I have provided consultancy (received payment for work) for Bayer on the topic of oral Anticoagulants on 13 May 2015.

Date: 16.11.16

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Declaration of Interest:

None to declare

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