Briefing Paper for Surrey Heartlands Integrated Care System (ICS) Area Prescribing Committee (APC)

NICE Technology Appraisals: Local implementation

NICE TA Guidance name and number	Brolucizumab treating diabetic macular oedema (TA820) Technology appraisal guidance 820 Fast track 30-day implementation.		
Available at	https://www.nice.org.uk/guidance/ta820		
Date of issue	31st August 2022	**Implementation deadline**	30th September 2022

Medicine details[1]	
Name, brand name and manufacturer	Brolucizumab (Beovu®) Novartis
Mode of action	www.nice.org.uk [accessed on 25/08/2022 at 1635] Brolucizumab is a humanised monoclonal single chain Fv (scFv) antibody fragment with a molecular weight of ~26 kDa. Increased levels of signalling through the vascular endothelial growth factor A (VEGF-A) pathway are associated with pathological ocular angiogenesis and retinal oedema. Brolucizumab binds with high affinity to VEGF-A isoforms (e.g. VEGF110, VEGF121, and VEGF165), thereby preventing binding of VEGF-A to its receptors VEGFR-1 and VEGFR-2. By inhibiting VEGF-A binding, brolucizumab suppresses endothelial cell proliferation, thereby reducing pathological neovascularisation and decreasing vascular permeability ***Committee discussion*** *Aflibercept and ranibizumab are anti-VEGFs recommended by NICE for treating DMO and accepted as comparators to brolucizumab.* *The External Assessment Group (EAG) confirmed that, based on clinical expert opinion, aflibercept and ranibizumab are the standard first line treatments for diabetic macular oedema.*
Licensed indication	www.medicines.org.uk [accessed on 25th August 2022 at 1640] Brolucizumab (Beovu®) 'is indicated in adults for the treatment of visual impairment due to diabetic macular oedema (DME)'
Formulation	Intravitreal injection.
Usual dosage	www.medicines.org.uk [accessed on 25th August 2022 at 1640] The recommended dose is 6 mg brolucizumab (0.05 ml solution) administered by intravitreal injection every 6 weeks for the first 5 doses. Thereafter, the physician may individualise treatment intervals based on disease activity as assessed by visual acuity and/or anatomical parameters. In patients without disease activity, treatment every 12 weeks (3 months) should be considered. In

	patients with disease activity, treatment every 8 weeks (2 months) should be considered. If visual and anatomical outcomes indicate that the patient is not benefiting from continued treatment, Beovu® should be discontinued.
Comparison with NICE TA use[2]	NICE TA sets out criteria for use i.e., as an option to use only if the eye has a central retinal thickness of 400 micrometres or more at the start of treatment. This is the same as for the other options, aflibercept and ranibizumab. No dosages or lengths of treatment are defined. *This is the current dose considered by NICE as part of this NICE evaluation. Subsequent changes in the license following NICE publication will need to be considered by the Area Prescribing Committee and **will not be routinely funded** by local commissioners.*

Disease and potential patient group	
Brief description of disease	https://www.moorfields.nhs.uk/sites/default/files/Diabetic%20macular%20oedema.pdf Diabetic eye disease is a leading cause of blindness registration among working age adults in England and Wales. It is caused by changes to the tiny blood vessels of the retina (the light sensitive layer at the back of the eye). In diabetic macular oedema, blood vessels leak fluid into the retina. Vision loss occurs when the fluid reaches the macula (the centre of the retina that provides sharp vision) and builds up, causing swelling. At first, you may not notice changes to your vision. Over time, diabetic macular oedema can cause your central vision to become blurred. A healthy macula is essential for good vision. All people with type 1 and type 2 diabetes are at risk of diabetic macular oedema.
Potential patient numbers per 100,0004	Information from the costing template anticipates the • Prevalence of visual impairment due to DME as 168/100,000 population. • With 44/100,000 as a proportion with central retinal thickness of 400 micrometres • With 11/100,000 as a proportion of prevalent population with a central retinal thickness of < 400 micrometres who change to more than or equal to 400micrometers each year • Eligible population for treatment with anti VEGFs 54/100,000

SUMMARY

Guidance[2]

1. Recommendations

1.1. Brolucizumab is recommended as an option for treating visual impairment due to diabetic macular oedema in adults, only if:

- the eye has a central retinal thickness of 400 micrometres or more at the start of treatment
- the company provides brolucizumab according to the commercial arrangement.

1.2. If patients and their clinicians consider brolucizumab to be 1 of a range of suitable

treatments (including aflibercept and ranibizumab), choose the least expensive treatment. Take account of administration costs, dosage, price per dose and commercial arrangements.

1.3. These recommendations are not intended to affect treatment with brolucizumab that was started in the NHS before this guidance was published. People having treatment outside these recommendations may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Diabetic macular oedema is usually treated first with aflibercept or ranibizumab, which are already recommended by NICE for treating diabetic macular oedema if the eye has a central retinal thickness of 400 micrometres or more when treatment starts. Brolucizumab is another treatment option that works in a similar way

Evidence from clinical trials shows that brolucizumab is as effective as aflibercept. An indirect comparison of brolucizumab with ranibizumab also suggests similar clinical effectiveness, although this is uncertain.

A cost comparison suggests brolucizumab has similar costs and overall health benefits to aflibercept or ranibizumab. So, brolucizumab is recommended for treating diabetic macular oedema if it is used in the same population as aflibercept and ranibizumab.

The NICE expert group (EAG) clinical experts reported potential safety concerns in terms of intraocular inflammation with brolucizumab. Also that brolucizumab may be used as a second line treatment with preference for aflibercept or ranibizumab as first-line therapy although the company reports there are no clinical data for second-line use of brolucizumab in DMO.

Other factors e.g. equality issues

There are no equality issues relevant to the recommendations.

Cost implications* [2,3,4]

Cost:
Brolucizumab costs £816 for 1 vial of 120 mg per 1 ml solution for injection (excluding VAT; BNF online, accessed July 2022).

The company has a commercial arrangement (simple discount patient access scheme). This makes brolucizumab available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

Annual or monthly cost per patient:
Information from the NICE resource template
https://www.nice.org.uk/guidance/ta820/resources

Unit costs/patient

Brolucizumab (Intravitreal injection)

Year	Dose mg	Average number of administrations needed in year (local input)	Proportion of people requiring treatment in both eyes (local input)	Average number of vials needed	Cost per 6 mg vial (local input)	Total cost of treatment exc. VAT	VAT rate	Total cost of treatment inc. VAT
Year 1	6	7.0	46.5%	10.3	£816	£8,368	20%	£10,042
Year 2	6	5.0	46.5%	7.3	£816	£5,977	20%	£7,173
Year 3	6	5.0	46.5%	7.3	£816	£5,977	20%	£7,173
Year 4	6	5.0	46.5%	7.3	£816	£5,977	20%	£7,173
Year 5	6	5.0	46.5%	7.3	£816	£5,977	20%	£7,173
						£20,322		**£24,387**

Year	Dose mg	Average number of administrations needed in year (local input)	Tariff (local input)	Average number of vials needed
Year 1	2022/23 National Tariff Payment System. Outpatient procedure, HRG code BZ87A Minor Vitreous Retinal Procedures, 19 years and over	7.0	£99	£693
Year 2		5.0	£99	£495
Year 3		5.0	£99	£495
Year 4		5.0	£99	£495
Year 5		5.0	£99	£495
				£1,683

**NICE funding requirements are based on Quality Adjusted Life Years (QALY) threshold. If there is evidence that the incremental cost rises above this threshold in the future, the APC may reconsider the commissioning status*

Patient Numbers:
Numbers are expected to be small because of the potential safety concerns in terms of intraocular inflammation with brolucizumab.
Assumptions have been made by NICE based on national data and the view of clinical experts advising NICE
The information below is taken directly from the NICE resource template /100,000 population.

	NICE assumptions current practice	NICE assumptions current practice	NICE assumptions future practice (year 5)	NICE assumptions future practice (year 5)
	% of people	Number of people	% of people	Number of people
Eligible population		54		54
Estimated market share for brolucizumab	0.00%	0	10.00%	5
Estimated market share for faricimab	15.00%	8	15.00%	8
Estimated market share for aflibercept	75.00%	41	70.00%	38
Estimated market share for ranibizumab	10.00%	5	5.00%	3

No significant resource impact is anticipated

We do not expect this guidance to have a significant impact on resources; that is, the resource impact of implementing the recommendations in England will be less than £5 million per year (or approximately £9,000 per 100,000 population, based on a population for England of 56.3 million people).

This is because the technology is a further treatment option and the overall cost of treatment has been proposed as being similar to aflibercept and ranibizumab.

The cost analysis is not very robust as the primary analysis covered the wider population of patients with DMO due to data limitations for patients with CRT ≥400 µm. The trials were powered for non-inferiority. They compared brolucizumab with regular doses of aflibercept (and not treat and extend as is the most cost-effective protocol), but the conclusions indicated that brolucizumab required fewer injections. It will only be real life experience which will determine whether brolucizumab is useful in patients who do not respond optimally to ranibizumab and/ or aflibercept.

Brolucizumab has a discount that is commercial in confidence. For enquiries about the patient access scheme contact commercial.team@novartis.com for details.

This technology is commissioned by integrated care systems. Providers are NHS Hospital Trusts.

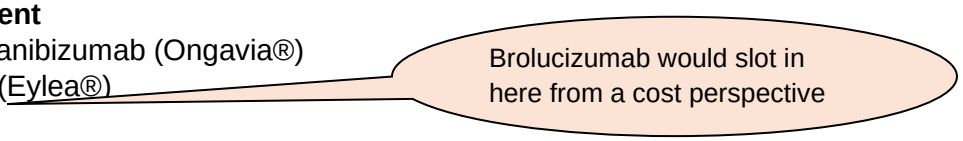
Availability of PAS and details (if appropriate):
Brolucizumab has a discount that is commercial in confidence.

Availability of homecare service (if appropriate
Yes

Alternative treatments and cost per patient per year

Other NICE recommended products: (listed in order of cost (commercially confidential))
Anti VEGF treatment

- Biosimilar ranibizumab (Ongavia®)
- Aflibercept (Eylea®)
- Faricimab
- Ranibizumab (Lucentis)



Intravitreal Corticosteroids – to be used in patients with a pseudophakic lens ('fake lens)

- Dexamethasone Intravitral implant (Ozurdex®) – for use when DMO does not respond to non-corticosteroid treatment, or such treatment is unsuitable.
- Fluocinolone acetonide intravitreal implant (Iluvien®) - for use when DMO is insufficiently responsive to available therapies

Options not reviewed by NICE but used in standard practice:
None

Impact to patients

- An additional treatment option would be valued by patients.

Impact to primary care prescribers

- This is a National Tariff excluded high-cost drug and is commissioned by integrated care systems (ICS) for use in secondary care. There should be no prescribing in primary care.
- Primary care prescribers should be aware that their patient is receiving this medicine and ensure that this is recorded in the patient's notes to be alert to potential side-effects and interactions with other medicines prescribed in primary care. This will also ensure that GP records, which are accessed by other healthcare providers, are a true and accurate reflection of the patient's medication.
- If patients present to their GP with retinal vasculitis will need to be seen immediately by the specialists as early treatment prevents blindness.

Impact to secondary care

- Providers are NHS hospital trusts.
- The initiation, administration and on-going treatment is managed by secondary care.
- An additional treatment option would be valued by clinicians.
- Secondary care will need to have a process to ensure patients understand the risk of vasculitis and react to it immediately seeking help.
- Specialists will need to have a process by which patients presenting with retinal vasculitis have urgent treatment to prevent blindness.

Impact to commissioners

- The technology is commissioned by ICBs and they are required to comply with the recommendations in a NICE TA within 30 days of its date of publication.

Implementation

- NICE TA fast track implementation must be within 30 days of publication.
- Blueteq forms to be developed.
- Trusts to follow internal governance procedures to add to their formulary.
- Pathway to be discussed at Ophthalmology Medicines Network and to consider the place

in the pathway.
- In order that brolucizumab can be used in the right place in therapy: where ranibizumab and/ or aflibercept has not achieved an optimal response, switching of anti-VEGF therapies for DMO needs to be proposed to the Area Prescribing Committee

Recommendation to APC

National Tariff excluded high-cost drug: Yes

Recommended traffic light status: RED

Additional comments: None

Area Prescribing Committee – Decision making criteria

National Guidance and priorities

- NICE published this Technology Appraisal (TA803) on 31st August 2022 with a 30-day implementation deadline (as opposed to the usual 90 days). Surrey Heartlands ICB is mandated to fund this treatment.

Clinical Effectiveness

- Evidence from clinical trials shows that brolucizumab is as effective as aflibercept. An indirect comparison of brolucizumab with ranibizumab also suggests similar clinical effectiveness, although this is uncertain.

- A cost comparison suggests brolucizumab has similar costs and overall health benefits to aflibercept or ranibizumab. So, brolucizumab is recommended for treating diabetic macular oedema if it is used in the same population as aflibercept and ranibizumab.

Patient Safety

- The NICE expert group (EAG) clinical experts reported potential safety concerns in terms of intraocular inflammation with brolucizumab.

Patient Factors

- An additional treatment option would be valued by patients.

Environmental impact

- Patients will be required to attend a clinic setting to receive the injection.

Equality and diversity

- The [NICE] committee did not identify any equality issues.

Place in therapy relative to available treatments

- Brolucizumab may be used as a second line treatment with preference for aflibercept or ranibizumab as first-line therapy although the company reports there are no clinical data for second-line use of brolucizumab in DMO.
- The Ophthalmology Medicines Network will be bringing a treatment pathway to the APC

Stakeholder views

- The Ophthalmology Medicines Network will receive this paper for comments during the wider APC consultation process.

Cost effectiveness

- We do not expect this guidance to have a significant impact on resources; that is, the resource impact of implementing the recommendations in England will be less than £5 million per year (or approximately £9,000 per 100,000 population, based on a population for England of 56.3 million people).
- This is because the technology is a further treatment option and the overall cost of treatment has been proposed as being similar to aflibercept and ranibizumab.

Additional funding required

- Anticipated cost is expected to be less than £100k/Place/annum financial threshold for APC decisions.

Identified implementation issues

- Discussion about place in therapy will be
- Drug should be identified as RED (hospital use only).
- GPs should continue to ensure patient practice records are kept up to date.

References:

1. **NICE Committee papers:** https://www.nice.org.uk/guidance/ta820/evidence/committee-papers-pdf-11193242221

2. **NICE guidance:** https://www.nice.org.uk/guidance/ta820

3. **Brolucizumab license: www.medicines.org.uk**

4. **Moorfield eye Hospital information on DMO** https://www.moorfields.nhs.uk/sites/default/files/Diabetic%20macular%20oedema.pdf

Declaration of interest: None