Surrey Heartlands Integrated Care System
Area Prescribing Committee (APC)

Integrated Care Partnership - Surrey Downs, Guildford & Waverley, North-West Surrey, and East Surrey Places & associated partner organisations.

NICE Technology Appraisals (TA) briefing paper for local implementation

NICE TA Guidance name and number	Bevacizumab gamma for treating wet age-related macular degeneration [TA1022]		
Available at	https://www.nice.org.uk/guidance/ta1022		
Date of issue	4th December 2024	**Implementation deadline**	30 days (3rd January 2024)

Medicine details	
Name and brand name	Bevacizumab gamma (Lytenava)
Manufacturer	Outlook Therapeutics
Mode of action	Bevacizumab gamma is a recombinant humanised IgG1 monoclonal antibody (mAb) for human vascular endothelial growth factor (VEGF).
Licenced indication	Bevacizumab gamma (Lytenava) is indicated in adults for treatment of neovascular (wet) age-related macular degeneration (nAMD).
Formulation	Bevacizumab gamma (Lytenava) 25 mg/mL solution for injection
Dosage	The recommended dose is 1.25 mg administered by intravitreal injection every 4 weeks (monthly). This corresponds to an injection volume of 0.05 mL. Treatment is initiated with one injection per month until maximum visual acuity is achieved and/or there are no signs of disease activity, i.e., no change in visual acuity or in other signs and symptoms of the disease under continued treatment. The kinetics of bevacizumab gamma efficacy, indicate that three or more consecutive monthly injections may be needed initially. Thereafter, the healthcare professional may individualise treatment intervals based on disease activity as assessed by visual acuity and/or anatomical parameters. Monitoring and treatment intervals should then be determined by the healthcare professional and should be based on disease activity, including clinical examination, functional testing or imaging techniques (e.g. optical coherence tomography or fluorescein angiography). If visual and anatomical outcomes indicate that the patient is not benefiting from continued treatment, the medicinal product should be discontinued. Treatment should also be withheld if clinically indicated,

Comparison of NICE TA with Summary of Product Characteristics (SmPC)	Licensed indication is for adult treatment of wet AMD. NICE (as per other anti-VEGF TAs) has been specific about when bevacizumab gamma should be used. This is the current dose considered by NICE as part of this NICE evaluation. Subsequent changes in the licence following NICE publication will need to be considered by the Area Prescribing Committee and will not be routinely funded by local commissioners, as the incremental cost per QALY would not have been considered.

NICE TA recommendations

Recommendations

1. Recommendations

1.1. Bevacizumab gamma is recommended as an option for treating wet age-related macular degeneration in adults, only if:

- the eye has a best-corrected visual acuity between 6/12 and 6/96
- there is no permanent structural damage to the central fovea
- the lesion size is 12 disc areas or less in greatest linear dimension
- there are signs of recent disease progression (for example, blood
- vessel growth as shown by fluorescein angiography, or recent visual
- acuity changes)
- the company provides it according to the commercial arrangement (see
- section 2).

1.2. Use the least expensive option of the available treatments (including bevacizumab gamma, aflibercept, faricimab and ranibizumab. Take account of administration costs, dosages, price per dose and commercial arrangements. If the least expensive option is unsuitable, people with the condition and their healthcare professional should discuss the advantages and disadvantages of other treatments.

1.3. Only continue bevacizumab gamma treatment if an adequate response is maintained. Criteria for stopping should include persistent deterioration in visual acuity and anatomical changes in the retina.

1.4. These recommendations are not intended to affect treatment with bevacizumab gamma 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 these recommendations were made

NICE already recommends aflibercept, faricimab and ranibizumab as treatment options for wet age-related macular degeneration. Bevacizumab gamma works in a similar way to these treatments and would be offered to the same population.

Evidence from clinical trials shows that more people having bevacizumab gamma gain at least 15 letters in best-corrected visual acuity than those having ranibizumab. And an indirect comparison of bevacizumab gamma with ranibizumab, aflibercept and faricimab suggests similar clinical effectiveness.

Using NICE's cost-comparison methods, bevacizumab gamma only needs to provide similar or greater health benefits at similar or lower costs to 1 relevant comparator to be recommended as a treatment option. The total cost of bevacizumab gamma is similar to the cost of aflibercept. So bevacizumab gamma is recommended.

For all evidence see the committee papers. For more information on NICE's evaluation of aflibercept, see the committee discussion section in NICE's technology appraisal guidance on aflibercept for treating wet age-related macular degeneration.

Decision making framework (DMF)

National guidance and priorities

The ICS has a legal obligation to commission this medicine in line with the NICE TA.

- This NICE TA has been assigned an implementation fast track deadline 30 days.
- The implementation deadline is 3rd January 2024

Clinical effectiveness

- Evidence from clinical trials shows that more people having bevacizumab gamma gain at least 15 letters in best-corrected visual acuity than those having ranibizumab. And an indirect comparison of bevacizumab gamma with ranibizumab, aflibercept and faricimab suggests similar clinical effectiveness.
- MRU comments - It is noted that the trials (NORSE ONE & TWO) evaluated by NICE, did not use the same treatment schedule for ranibizumab and bevacizumab and so the conclusion, also in NICE (above), should be noted that all treatments suggest similar clinical effectiveness rather than bevacizumab gamma being superior to ranibizumab.

Patient safety

- The product should be used within its product licence.
- ▼ This is a Black Triangle drug – this medicinal product is subject to reporting of all suspected adverse drug reactions to the MHRA. This will allow timely identification of new safety information.
- There are or no additional safety concerns identified outside those already recognised and described in BNF / SPC.
- Bevacizumab gamma is in a vial and aseptic technique will need to withdraw the contents of the vial for injection.

Patient factors

- An additional treatment option would be valued by patients. however, there are 4 other anti-VEGF treatments already in the available pathway, so it does not constitute a novel mode of action or a new line of treatment.
- Patients will be treated with one injection per month (every 4 weeks) until maximum visual acuity is achieved and/or there are no signs of disease activity.
- Patients would need to be reviewed on a regular basis by the prescribing clinician to ensure concordance, monitor for adverse effects and efficacy.

Environmental impact

- Additional packaging will be generated and will be an environmental impact with regards to waste management.
- Sharps waste requires safe collection and disposal

Equality & diversity

Age

- Bevacizumab gamma is only licensed for use in adults
- NICE costing template uses population of adults over 50 years of age.
- Women of child-bearing potential should use effective contraception during treatment for at least 3 months after the last dose when stopping treatment with bevacizumab gamma.

Being pregnant or on maternity leave

- Bevacizumab gamma should not be used during pregnancy unless the potential benefit outweighs the potential risk to the foetus.

Disability

- People that are 'housebound' and unable to travel to receive the intravitreal injections will potentially be given sub optimal treatment.
- Anti- VEGF treatment should be carried out under aseptic conditions.

Note 1: Drugs approved by NICE for adult conditions will be commissioned in children at specialised paediatric centres if the patient meets the NICE criteria and there is evidence to suggest that the drug is safe and clinically appropriate to use in children as per the NHS England Medicines for Children Policy (see https://www.england.nhs.uk/publication/commissioning-medicines-for-children-specialised-services/ and a Blueteq form is available.

Place in therapy relative to available treatments

- In 2018 the APC agreed that bevacizumab 1.25mg would be a cost-effective treatment option, alongside ranibizumab or aflibercept, for patients with Wet Age-Related macular Degeneration (wet AMD) **who met NICE guidance** for anti VEGF treatment. The decision made in 2018 also approved that bevacizumab could also be offered to individuals, after discussion of treatment options, for those patients with visual acuity **outside of NICE.**
- In total 57 notifications of treatment with off label bevacizumab have been received for Surrey Heartlands residents **OUTSIDE NICE THRESHOLDS,** since January 2020.

Stakeholder views

- The briefing paper has been circulated to the Ophthalmology Medicines Network for their views prior to APC consideration
- Comments will be included in the front cover.

Cost-effectiveness

Cost of the technology

- The list price of bevacizumab gamma is £470 for 1 vial of 7.5mg per 0.3ml solution. (excluding VAT)

a. Annual cost per patient (or complete course if shorter)

- The recommended dose is on intravitreal injection every 4 weeks (monthly) into the affected eye so a patient could receive a maximum of 13 injections per year.
- Total cost per 1 year of treatment in a single eye = £6,110 (excluding VAT)
- There will be no cost impact in primary care. Bevacizumab gamma will be given under specialist supervision in secondary care.

b. Availability of CAP/PAS price:

- Yes
- Bevacizumab gamma from a pricing perspective is more expensive then ranibizumab biosimilar but cheaper than aflibercept, faricimab & brolucizumab.

c. Price relative to comparable medicines:

- Ranibizumab biosimilar is the least costly preparation used in the wet AMD pathway and specialists are encouraged to use this treatment 1st line, if capacity in clinics allows and if patients require monthly injections.
- Biosimilar aflibercept is expected to be available from Q3 2025/26 there are expected to be significant windfall savings as patients are switched from the originator (Eylea®) to the biosimilar product.
- Treat and Extend protocols should be considered as appropriate (information available in the wet AMD pathway).
- Treat and Extend protocols were not studied in the main bevacizumab gamma trials (NORSE ONE & TWO), however previous studies with ranibizumab & off label bevacizumab used treat-and-extend by 2 weekly increments (up to 1 injection/12 weeks) for ranibizumab and for off label bevacizumab[1][2]

The Surrey Heartlands Director of Pharmacy and Medicines Optimisation has delegated authority to enable the Committee to be a decision-making committee providing the impact of any single decision does not exceed £100,000 within an individual Place per annum. Decisions with a cost impact of over £100,000 within an individual Place per annum require authorisation from Surrey Heartlands Health & Care Professionals Committee at their next meeting. Exception to this will be for any decision made in relation to a NICE Technology Appraisal (which are subject to requiring mandatory funding by commissioners) and other urgent items. The exceptions will be taken to the next Executive Meeting (which meets weekly) for authorisation.

[1] Berg K, Pedersen TR, Sandvik L, et al. Comparison of ranibizumab and bevacizumab for neovascular age-related macular degeneration according to LUCAS treat-and-extend protocol. *Ophthalmology* 2015; 122:146–152.

[2] Berg K, Hadzalic E, Gjertsen I, et al. Ranibizumab or bevacizumab for neovascular age-related macular degeneration according to the Lucentis Compared to Avastin Study treat-and-extend protocol: two-year results. Ophthalmology 2016; 123:51–59.

Traffic light recommendation to APC

NHS Payment Scheme (NHSPS) excluded high-cost drug: see NHS England » 2023-25 NHS Payment Scheme

- Yes

Recommended traffic light status and rationale:

RED traffic light status

- Intravitreal Injection - treatment initiated and continued by specialist clinicians.

Implementation

NICE TA implementation must be within 30days of publication.

Actions to implement:
Consider the following in the appropriate sections below to define actions to implement the NICE TA:

- a need for starting criteria, monitoring parameters, stopping criteria.
- place in therapy – current guidelines need updating/new guidelines or pathway required?
- any possible deprescribing or decommissioning?
- any barriers to implementation locally?
- is there a cohort of patients that will need special consideration e.g., transition patients?

Primary care

- This is a National Tariff excluded high-cost drug and is commissioned by ICSs 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 in order 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.

Secondary care

- Providers are NHS hospital trusts.
- Bevacizumab gamma must be administered by a qualified healthcare professional,
- experienced in intravitreal injections.
- The initiation, administration and on-going treatment is managed by secondary care.
- Trusts to follow internal governance procedures to add to their formulary and initiate homecare.
- Specialists will be required to notify the high-cost drugs teams of initiation of treatment using the Blueteq® system.
- Bevacizumab gamma must be stored in a refrigerator (as all the anti-VEGF treatments in the wet AMD pathway)
- Bevacizumab gamma is in a vial and aseptic technique will need to withdraw the contents of the vial for injection. All other anti-VEGF treatments are available in a pre-filled syringe.

ICS

- This technology is commissioned by integrated care systems and they are required to comply with the recommendation in the NICE TA within the time set in the publication.
- Proposed pathway to be discussed with the Ophthalmology Medicines Network

PAD and Joint Formulary

- New PAD guidelines profile for wet AMD required
- Upload updated guidelines to that page on PAD
- Upload decision to newly developed bevacizumab gamma profile page

Proposed tick box forms

Blueteq® forms have been developed.

References:

1 Summary of Product Characteristics. emc. Available at: www.medicines.org.uk Accessed < 4th December 2024>

2 NICE Technology Appraisal Guidance: Available at: www.nice.org.uk Accessed < 4th December 2024>

3 NICE Resource Impact Report: Available at: www.nice.org.uk Accessed < 4th December 2024

4 NICE Resource Impact Template: Available at: www.nice.org.uk Accessed < 4th December 2024>

Declaration of interest:

	Name	Role	Date	Declaration of interests (please give details below)
Prepared by	Clare Johns	Lead Pharmacy Technician – Medicines Resource Unit	4th December 2024	None
Supported by				
Reviewed by				

Explanation of declaration of interest:
None.