A national framework for implementing Beovu (brolucizumab) in the treatment of patients with neovascular age-related macular degeneration: An expert consensus

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INTRODUCTION

- Brolucizumab is a monoclonal antibody, which binds to VEGF-A and reduces neovascularisation.[8,9]
- The efficacy and safety of brolucizumab has been assessed in two Phase 3 trials, HAWK and HARRIER, in patients with nAMD.[10,11] Brolucizumab subsequently received marketing authorisation from European Medicines Agency (EMA) and NICE approval.[8,9]
- Introducing a new treatment into the clinic can be challenging, especially in services that are already under significant time and capacity burden.
- We aim to provide recommendations from evidence-based review and guidance for the practical implementation of brolucizumab for the treatment of patients with nAMD to United Kingdom (UK) medical retina services.

METHODS

- A working group of MR experts with experience of leading and managing NHS retinal services in the intravitreal era covering a reasonable geographic spread across England was established.
- Roundtable meetings were conducted between February 2020 and August 2021, facilitated by Novartis UK.
- The meetings explored and discussed the key aspects of delivering anti-VEGF therapy and in particular brolucizumab to UK medical retina services.
- This led to the development of guidance on the practical implementation of brolucizumab in UK medical retina services.

RESULTS

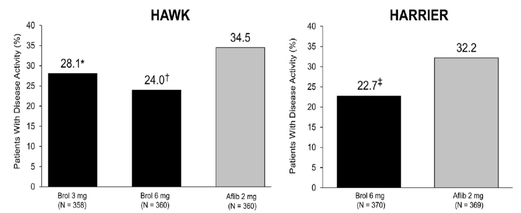
Patient populations

- Based on NICE guidance and clinical trial outcomes brolucizumab is recommended for patients with confirmed diagnosis of nAMD and for whom there are no contraindications (**Table 1**).[8-11]
- Whilst any new patient with progressive nAMD is potentially eligible for brolucizumab a practical stratified introduction of brolucizumab in clinical practice is advised (**Table 1**).
- When deciding on the patient population for brolucizumab treatment it is worth considering a pragmatic approach to use in patients keen to avoid frequent injections or frequent visits to the clinic or patients who may have difficulty attending regular fundus examinations (**Table 1**).

Table 1. Patient populations

Contraindications for all intravitreal anti-VEGF therapies[8,12,13]	
Contraindications for intravitreal anti-VEGF therapies	• Hypersensitivity to active substance or any excipients • Patients with active or severe intraocular inflammation (previous history of anterior uveitis is not considered an exclusion criterion) • Active or suspected ocular or periocular infections
Expert considerations for initiating treatment with brolucizumab in nAMD patients	
Clinical experts highlighted cautionary criteria to consider when choosing brolucizumab	• Patients with prior history of retinal vasculitis or arterial occlusion • Eyes with active scleritis and episcleritis may be excluded at the discretion of the treating physician • History of any intraocular inflammation • Previous culture-negative endophthalmitis • The evidence on efficacy and adverse events of brolucizumab is continually evolving; there is a need to review the data and seek advice as necessary from senior consultants

Figure 1. Disease activity at Week 16 (HAWK and HARRIER trial)



***The 95% confidence interval (CI) for treatment difference, −13.2 to 0.3; p=0.033. †95% CI for treatment difference, −17.1 to −3.5; p=0.001. ‡95% CI for treatment difference, −15.8 to −3.1; p=0.002. 1-sided p-values versus aflibercept. CI, confidence interval.**

Informed Consent

- **Patient-centered dialogue** is important, and these discussions help highlight the benefit:risk for brolucizumab treatment.
- Opportunity to put the information into context e.g., explaining the **overall inflammation and vision loss is not per injection but based on 2 years treatment as per the clinical trials.**[10,11]

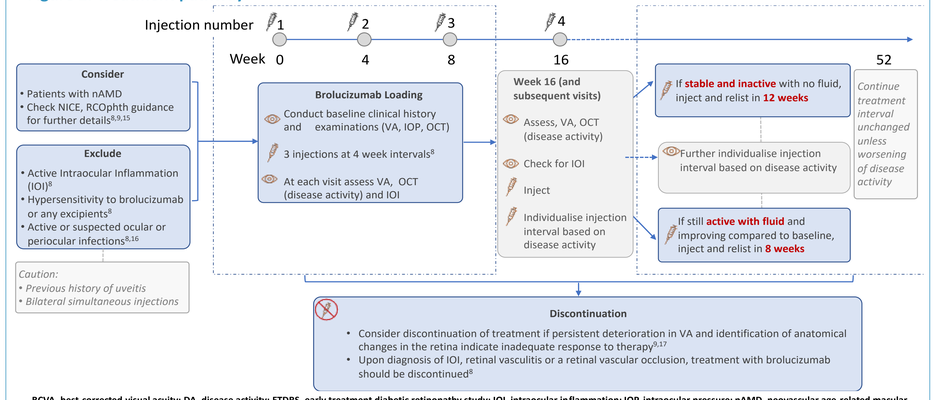
Benefit considerations

- In HAWK/HARRIER brolucizumab (6 mg) demonstrated:[8,10,11]
  - **Non-inferiority with respect to BCVA** change from baseline to Week 48 vs aflibercept with greater than 50% of brolucizumab 6 mg treated eyes maintained on q12w dosing through Week 48 (56% [HAWK] and 51% [HARRIER]).
  - **Greater CST reductions and significantly fewer patients with IRF and/or SRF** vs aflibercept throughout the the study,
  - At Week 16, after identical treatment exposure, fewer brolucizumab 6 mg–treated eyes had disease activity versus aflibercept (24.0% vs. 34.5%; p=0.001 and 22.7% vs. 32.2%; p=0.002, HAWK/HARRIER respectively, **Figure 1**).

Mitigation and management of risks

- Key AEs of interest include intraocular inflammation (IOI) (4.6%), retinal vasculitis (3.3%), and concomitant retinal vasculitis and retinal vascular occlusion (2.1%).[14]
- Over two years,
  - The absolute risk of developing IOI of any form was 4.6%
  - The risk of moderate/severe visual loss due to IOI (≥15 letters) was 0.7%.[14]
- Pragmatic approach to monitoring and assessing for IOI at each scheduled visit in conjunction with educating patients to self-monitor.
- Educate patients to report symptoms as they arise, which Is vital for early diagnosis.
- Evaluation for potential side effects (e.g., IOI), together with visual acuity (VA) and anatomy on Optical Coherence Tomography (OCT) imaging is recommended at each scheduled visit.
- Retinal examination at the slit lamp or wide-field imaging at clinician discretion.
- Risk of inflammatory event is reduced after 6 months but checks are recommended at each visit.

Figure 2. Treatment pathway



BCVA, best-corrected visual acuity; DA, disease activity; ETDRS, early treatment diabetic retinopathy study; IOI, intraocular inflammation; IOP, intraocular pressure; nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography; RO, retinal vascular occlusion; VA, visual acuity.

CONCLUSIONS

- Based on NICE guidance and clinical trial outcomes brolucizumab is recommended for patients with confirmed diagnosis of nAMD and for who there are no contraindications[8–11]
- Brolucizumab offers clinicians another therapy in the armamentarium that could be of benefit to overcoming and addressing the unmet needs and challenges currently faced by patients and medical retina services (**Figure 2**)
- Patient-centered dialogue is important to help emphasise the benefit:risks of brolucizumab treatment
- When deciding on the patient population for brolucizumab treatment it is worth considering a pragmatic, individualised approach to use in patients with nAMD
- The most pragmatic approach is for patients to be monitored and assessed for IOI at each scheduled visit in conjunction with educating the patient to self-monitor
- Checks for side effects, visual acuity and anatomy on OCT scans are recommended at each treatment visit to help optimally guide future treatment, although full disease activity assessments are not essential at all visits
- The potential benefit of brolucizumab for the treatment of patients with nAMD has been demonstrated in the HAWK and HARRIER, randomised, phase 3 clinical trials[10,11]

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