Dual Pathway Inhibition With Faricimab for Previously Treated Neovascular Age-Related Macular Degeneration and Diabetic Macular Oedema: Guidance From a UK Panel of Retina Specialists

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Purpose

To provide clinician-led practical guidance for switching patients with suboptimal response to previous intravitreal anti–vascular endothelial growth factor (VEGF) treatment for neovascular age-related macular degeneration (nAMD) and diabetic macular oedema (DMO) to dual angiopoietin (Ang)-2/VEGF inhibition with faricimab

Conclusions

Clinicians may consider a treatment switch to faricimab in patients with nAMD and DMO who have suboptimal disease control or insufficient durability on initial anti-VEGF monotherapy

Disease control and frequency of injections should be at the forefront of clinician thinking when assessing treatment response and switch strategies in the management of patients with nAMD and DMO

Additionally, decreased injection frequency across a subset of patients may help to improve clinic capacity, thereby preventing treatment delays and potentially facilitating implementation of new or additional services[1]

Current clinician guidance on switch strategies may be further adapted as additional longer-term data and evidence emerge from multiple, ongoing real-world studies[2-4]

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- JS: Consultancy: Bayer, Roche
- SLW: Consultancy and Honoraria: Bayer, Novartis, Roche
- GW: Honoraria: Roche
- SE: Honoraria and Travel Support: AbbVie, Alimera, Bayer, Novartis, Roche, Topcon
- SK, AP: Employee: Roche Products Ltd.

Study and Product Disclosures

- In the UK, faricimab is approved for the treatment of neovascular age-related macular degeneration and diabetic macular oedema. Faricimab is not currently approved for use outside these indications in the UK
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Introduction

- Some eyes with nAMD and DMO fail to respond sufficiently or lose response over time to standard of care anti-VEGF therapy and require review to assess alternative or additional treatment[5-7]
- Faricimab (Vabysmo®), approved in the United Kingdom in 2022 for the treatment of nAMD and DMO, represents an additional effective treatment option[8]
- Faricimab is a bispecific antibody that acts through inhibition of 2 distinct pathways by neutralisation of both Ang-2 and VEGF-A[8]
- Ang-2 inhibition in combination with VEGF inhibition may promote vascular stability beyond anti-VEGF therapy alone[9-12]

Methods

- A national steering group meeting of 11 UK medical retina specialists and 2 Roche Products Ltd. medical affairs partners was held in London on 27 October 2023
- The meeting was facilitated and funded by Roche Products Ltd.
- The panel reviewed data from the pivotal faricimab clinical trials and evidence from post hoc exploratory analyses, and considered current clinical practice, experience and opinion with respect to:
  - Clinical biomarkers and effectiveness outcomes relevant to assessment of patient response to anti-VEGF treatment; and
  - Strategies for switching to faricimab as an additional option for patients with suboptimal improvement on initial anti-VEGF treatment

References

1. Narayan A et al. Presented at: Royal College of Ophthalmologists Annual Meeting; 25–28 May 2023; Birmingham, UK.
2. Talks J et al. Presented at: 23rd European Society of Retina Specialists Congress; 5–8 October 2023; Amsterdam, The Netherlands.
3. Bailey C et al. Presented at: 23rd European Society of Retina Specialists Congress; 5–8 October 2023; Amsterdam, The Netherlands.
4. Penha FM et al. *Int J Retina Vitreous*. 2024;10(1):5.
5. Wallsh JO, Gallemore RP. *Cells*. 2021;10(5):1049.
6. Khachigian LM. *J Transl Med*. 2023;21(1):133.
7. Sharma D et al. *Invest Ophthalmol Vis Sci*. 2023;64(5):28.
8. Vabysmo 120 mg/mL solution for injection [Summary of Product Characteristics]. Welwyn Garden City, UK: Roche Products Ltd.; January 2024.
9. Khanani AM et al. *Clin Ophthalmol*. 2021;15:3747-3755.
10. Regula JT et al. *EMBO Mol Med*. 2016;8(11):1265-1288.
11. Joussen AM et al. *Eye (Lond)*. 2021;35:1305-1316.
12. Heier JS et al. *Retina*. 2021;41(1):1-19.
13. Hanson RLW et al. *Eye (Lond)*. 2023;37(12):2438-2453.
14. Bailey C et al. *Eye (Lond)*. 2023;37(9):1916-1921.
15. Kodjikian L et al. *Eye (Lond)*. 2021;35(8):2119-2135.
16. National Institute for Health and Care Excellence. *Faricimab for treating diabetic macular oedema (TA799). Technology appraisal guidance*. NICE; 29 June 2022. www.nice.org.uk/guidance/ta799
17. National Institute for Health and Care Excellence. *Guideline. Diabetic retinopathy: management and monitoring. Draft for consultation*. NICE; August 2023.
18. Khanani AM et al. Presented at: Angiogenesis, Exudation, and Degeneration 2023 Virtual Meeting; 10–11 February 2023.

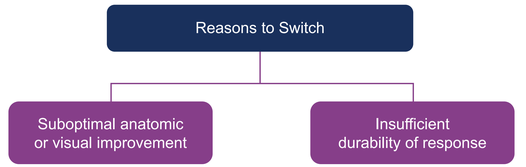
Results

Signs of Disease Activity to Guide Re-Treatment Decisions

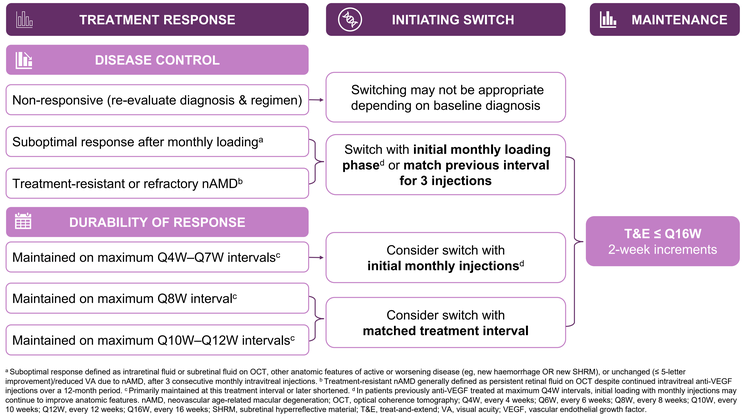
	Biomarker on OCT					Visual Acuity
	IRF and/or SRF	CST or CRT	Macular Haemorrhage	SHRM	PED	
nAMD	New or increased[13]	Increased or persistent	New or increased	New or increased[13]	Increased size[13]	Decrease of ≥ 5 ETDRS letters attributable to CNV activity[14,15]
DMO	New or increased	< 20% reduction or CRT ≥390 µm[a,16]				Decrease of ≥ 5 ETDRS letters attributable to DMO

[a] Practical threshold for defining insufficient anatomic response as a reduction of less than 20% in reference CST/CRT (documented for example at time of diagnosis) and/or retinal thickness above an indicative absolute CST/CRT value or threshold as determined by the treating clinician (eg, 390 µm if NICE guidance recommendation of CRT criterion of ≥ 400 µm was used to initiate anti-VEGF treatment). CNV, choroidal neovascularisation; CRT, central retinal thickness; CST, central subfield thickness; DMO, diabetic macular oedema; ETDRS, Early Treatment Diabetic Retinopathy Study; IRF, intraretinal fluid; nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography; PED, pigment epithelial detachment; SHRM, subretinal hyperreflective material; SRF, subretinal fluid.

Common Reasons for Considering a Change of Treatment

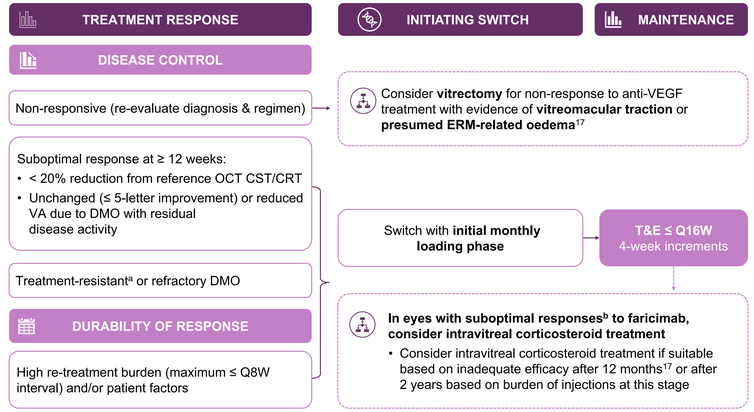


Guidance for Switching to Faricimab in Previously Treated nAMD



[a] Suboptimal response defined as intraretinal fluid or subretinal fluid on OCT, other anatomic features of active or worsening disease (eg, new haemorrhage OR new SHRM), or unchanged (≤ 5-letter improvement)/reduced VA due to nAMD, after 3 consecutive monthly intravitreal injections. [b] Treatment-resistant nAMD generally defined as persistent retinal fluid on OCT despite continued intravitreal anti-VEGF injections over a 12-month period. [c] Primarily maintained at this treatment interval or later shortened. [d] In patients previously anti-VEGF treated at maximum Q4W intervals, initial loading with monthly injections may continue to improve anatomic features. nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography; Q4W, every 4 weeks; Q8W, every 8 weeks; Q8W, every 8 weeks; Q10W, every 10 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks; SHRM, subretinal hyperreflective material; T&E, treat-and-extend; VA, visual acuity; VEGF, vascular endothelial growth factor.

Guidance for Switching to Faricimab in Previously Treated DMO



[a] Treatment-resistant DMO generally defined as persistent DMO, increased retinal thickness, or unchanged (≤ 5-letter improvement)/reduced VA due to DMO with residual disease activity, despite continued intravitreal anti-VEGF treatment over a 12-month period. [b] Macular laser may be considered as adjunct therapy.[17] CRT, central retinal thickness; CST, central subfield thickness; DMO, diabetic macular oedema; ERM, epiretinal membrane; OCT, optical coherence tomography; Q10W, every 10 weeks; Q16W, every 16 weeks; T&E, treat-and-extend; VA, visual acuity; VEGF, vascular endothelial growth factor.

General Considerations When Switching

Bilateral Involvement

- Recommendation to switch both eyes at the same time if the same anti-VEGF agent is used
- If bilateral injections are planned for the same visit, a separate batch of medication for each eye should be used
- Safety and efficacy of faricimab administered in both eyes concurrently have not been studied

Patient Counselling and Consent

- Patients should be informed of potential serious risks of IVT procedures and of VEGF inhibitors
- IOI rates in phase 3 clinical trials were low and comparable to aflibercept[18]; cases of retinal vasculitis/retinal occlusive vasculitis are rare
- For patients with nAMD, PED height ≥ 600 µm might have an increased risk of RPE tear
- Recommendation to repeat written consent if there is a change to treatment plan or drug used, clinical condition, and/or perceived risk/benefit to the patient
- Some patients may need a period of monthly faricimab dosing after a loading phase to maximise treatment response

Post Switch

- Patients who experience hypersensitivity or worsening anatomic response following a treatment switch to faricimab could either be switched back to previous anti-VEGF or given a different anti-VEGF agent

Modelling of Treatment Regimens

- Clinical modelling of alternative treatments and regimens should ideally capture a range of related healthcare costs and benefits for the patient, the practice and the healthcare system, including:
  - Net acquisition, administration and monitoring cost of therapy
  - Healthcare resource use and costs (OCT procedures, non-consultant-led outpatient visits, nurse- or technician-led monitoring, consultant-led reviews, post-injection management and overall episode costs)
  - Capacity improvements over time, supported by modelling assumptions of injection frequencies through years 3–5
  - Impact on patients and their carers

IOI, intraocular inflammation; IVT, intravitreal; nAMD, neovascular age-related macular degeneration; OCT, optical coherence tomography; PED, pigment epithelial detachment; RPE, retinal pigment epithelium; VEGF, vascular endothelial growth factor.