# Intravitreal faricimab for Diabetic Macular Oedema: Consensus Pathway by an Expert Panel of UK Retina Specialists

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* Roche medical affairs specialists contributing to roundtable discussions but not members of the expert panel

## Key Clinical Question

What are the recommendations and guidelines for implementing faricimab into routine clinical practice for patients with Diabetic Macular Oedema (DMO)?

## Introduction

- Faricimab is recommended by NICE as an option for treating adults with visual impairment due to DMO and the eye has a central retinal thickness of ≥400 µm at the start of treatment[1]
- In September 2022 and January 2023, roundtable meetings with an expert panel of UK retina specialists were held to update the current consensus on the treatment of adult patients with visual impairment due to DMO and review pivotal clinical trial results evaluating faricimab for DMO, the faricimab marketing authorisation and National Institute for Health and Care Excellence (NICE) technology appraisal guidance.
- The expert panel developed a consensus statement based on collective clinical experience in the treatment of DMO and suggested pathway recommendations for integrating faricimab for the management of DMO into UK clinical practice, as part of evolving medical retina treatment protocols. This poster summarises the expert panel's consensus recommendations.
- The expert panel meetings, as well as this publication and its development, were commissioned and funded by Roche Products Ltd.

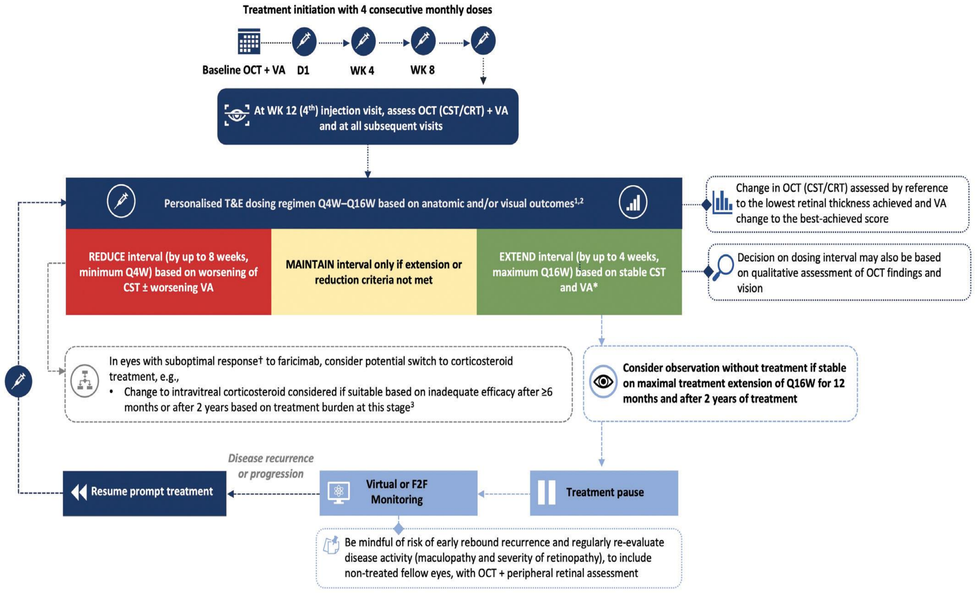
## Methods

- The National DMO Consensus Statement was published in Ophthalmology Times Europe May 2023.
- The expert panel of UK retina specialists created consensus for:
  - Integrating faricimab for DMO into clinical practice such as current practice in the management of treatment naïve patients with centre involved DMO
  - Posology for integrating faricimab into existing DMO treatment pathways for anti-VEGF naïve patients
  - Switching considerations and switching to faricimab
  - Determining suboptimal or insufficient response to initial therapy for DMO and treatment suspension or pause.
  - Review of pivotal clinical trial data, marketing authorisation and NICE guidance

## Conclusions

- Faricimab is a promising addition to the clinician's armamentarium of therapies for DMO which is effective, durable, and well tolerated, with approximately 80% of patients reaching Q12W dosing or longer in clinical trials
- Treatment with faricimab offers the potential to reduce the burden of injections and visits for patients, caregivers and clinics while maintaining optimal visual acuity and anatomic outcomes.
- A personalised T&E pathway for faricimab in DMO has been proposed by a panel of UK specialists to inform and guide implementation in clinical practice.
- The panel addressed three key areas of faricimab therapy: posology, determining treatment response and diagnostic criteria for suboptimal response

## 1. Recommended Intravitreal faricimab T&E pathway for the treatment of anti-VEGF naïve patients with DMO[2]




*In YOSEMITE and RHINE DMO trials, absence of DMO was defined as CST less than 325 µm. Patients in the faricimab personalised treatment interval arms received faricimab Q4W until they first reached a CST <325 µm at or after week 12; once achieved, adjustable dosing up to Q16W based on change in CST and BCVA values. †Laser may be considered as adjunct therapy.

BCVA, best-corrected visual acuity; CMH, Cochran-Mantel-Haenszel; IRF, intraretinal fluid; PTI, personalised treatment interval; Q8W, every 8 weeks; Q16W, every 16 weeks; SRF, subretinal fluid; VEGF, vascular endothelial growth factor; AE, adverse event; APTC, Antiplatelet Trialists' Collaboration; T&E, treat-and-extend. Anti-VEGF, anti-vascular endothelial growth factor; CRT, central retinal thickness; CST, central subfield thickness; D1, day 1; DMO, diabetic macular oedema; F2F, face to face; OCT, optical coherence tomography; Q4W, every 4 weeks; Q8W, every 8 weeks; SD-OCT, spectral domain OCT; VA, visual acuity; WK, week; NICE, National Institute of Clinical Excellence

## 2. General considerations and implementation recommendations

### Current practice in the management of treatment-naïve patients with centre-involved DMO

- Treatment of DMO with IVT anti-VEGF therapy should be initiated with the recommended phase of consecutive monthly injections and continued thereafter using a flexible individualised dosing regimen. Treatment decisions are mainly based on comparison of OCT findings and VA with best-achieved values or with those recorded at recent visits. In clinical practice, dosing interval extension is generally appropriate once CST or CRT on SD-OCT and VA are stable.
- The panel recommended that change in CST should be assessed by reference to the lowest CST achieved and VA change to the best-achieved score in response to treatment. It is important to be mindful of the absolute CST achieved and the subjective aspects of visual acuity measurements.
- The Diabetic Retinopathy Clinical Research Network (DRCR.net) anti-VEGF retreatment algorithm provides practical thresholds for determining improvement or worsening in response to treatment, assessments compared with the previous 2 or more visits[3]:
  - *Improvement: a decrease =10% in retinal thickness or an increase =5 in visual acuity letter score;*
  - *Worsening: an increase =10% in retinal thickness or a decrease =5 in visual acuity letter score; and*
  - *Stability: 2 consecutive visits without improvement or worsening of CST and vision.*
- Continued monitoring of maculopathy and retinopathy grade following baseline assessment is recommended and clinical examinations should include fellow eyes without DMO; the maximum review interval suggested by the panel was 4 months.
- The panel emphasised that clinicians should remain particularly focused on the need for appropriate metabolic control, especially of hypertension. Despite limited real-world experience, the panel considered that in line with other anti-angiogenic therapies, DMO patients with HbA1c above 10% may benefit from treatment with faricimab.[4]

### Integrating faricimab into existing DMO treatment pathways

- When starting treatment with faricimab, adhere to the recommended posology of 4 consecutive monthly doses followed by repeat injections with gradually extended dosing intervals up to every 16 weeks (Q16W), depending on disease activity and using a personalised T&E approach[5] .OCT and VA assessment at week 12 should be documented to provide a reference point to aid decision making.
- Extension increments of 4 weeks based on anatomic and/or visual outcomes are considered feasible and readily adoptable in clinic pathways. Interval reductions of 4 weeks and rarely 8 weeks (to minimum of Q4W) may be required if anatomic and/or visual outcomes deteriorate.

### Determining suboptimal or insufficient response to initial therapy for DMO

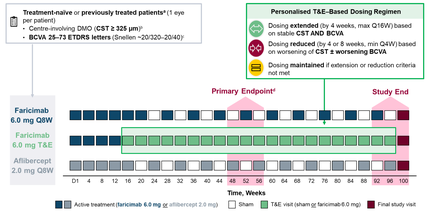
- For non-responders or insufficient response, clinicians need to ensure that appropriate treatment was administered (including appropriate treatment frequency) and should also consider alternative diagnosis and additional multimodal imaging to confirm DMO in these cases.
- A group of UK clinical experts suggested that a preliminary assessment of response to DMO treatment may be made one month after the recommended initial phase of monthly injections: a reduction from baseline in CST of less than 20% on OCT may be considered a suboptimal or poor response.[6]
- A change in therapy should be considered for DMO eyes showing <20% reduction in CRT on OCT and <5-letter improvement in visual acuity from baseline, according to guideline recommendations by a separate group of UK clinical experts.[7]

### Treatment suspension or pause

- Clinicians may consider a pause in treatment after a minimum of 2 years' treatment and if the patient appears stable on maximal treatment extension (Q16W) at consecutive visits for at least 12 months.
- DMO requires long-term treatment, re-evaluation at 2 to 4 months after treatment suspension to gauge maculopathy and the severity of retinopathy is recommended, as there can occasionally be rapid progression of proliferative disease following cessation.
- Regular ongoing monitoring (virtual or clinic) with SD-OCT and peripheral retinal assessment, using widefield imaging if available, is recommended.

YOSEMITE (NCT03622580; N = 940) and RHINE (NCT03622593; N = 951) are identical, randomised, double-masked, active comparator-controlled trials of faricimab in treatment-naïve and previously anti-VEGF–treated patients with DMO[8]

### YOSEMITE and RHINE Trial Design: Faricimab DMO Trials Use Disease Criteria Reflective of Clinical Practice[8]




*Previously anti-VEGF–treated eyes (treated ≥ 3 months before day 1) were limited to 25% of the total enrolment. †Primary efficacy endpoint: adjusted mean BCVA change from baseline at 1 year, averaged over weeks 48, 52 and 56. ‡CST was measured as the distance from the internal limiting membrane to Bruch's membrane. §Reference BCVA was defined as the mean of the 3 best BCVA values achieved at any prior active dosing visit. ¶Reference CST was defined as the CST value when the original reference value (CST + 325 µm) was achieved. Reference CST was adjusted if CST decreased by > 10% from the previous reference CST for 2 consecutive active dosing visits and the values obtained were within 30 µm. The CST value obtained at the latter visit served as the new reference CST.

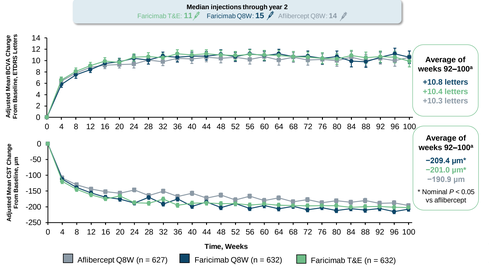
### Faricimab Was Well Tolerated Through Study End

| AEs Through Study End, Patients With ≥ 1 AE, n (%)[a] | YOSEMITE/RHINE Pooled | | |
|---|---|---|---|
| | Faricimab Q8W n = 630 | Faricimab T&E n = 632 | Aflibercept Q8W n = 625 |
| **Ocular AEs[b]** | 313 (49.7%) | 311 (49.2%) | 284 (45.4%) |
| **Serious ocular AEs[b]** | 26 (4.1%) | 34 (5.4%) | 20 (3.2%) |
| **Ocular AEs of special interest[c]** | 25 (4.0%) | 33 (5.2%) | 20 (3.2%) |
| **Intraocular inflammation events[d]** | 9 (1.4%) | 11 (1.7%) | 7 (1.1%) |
| Uveitis | 3 (0.5%) | 4 (0.6%) | 0 |
| Iritis | 1 (0.2%) | 4 (0.6%) | 2 (0.3%) |
| Iridocyclitis | 2 (0.3%) | 3 (0.5%) | 1 (0.2%) |
| Vitritis | 2 (0.3%) | 0 | 2 (0.3%) |
| Post-procedural inflammation | 1 (0.2%) | 1 (0.2%) | 2 (0.3%) |
| Chorioretinitis | 0 | 1 (0.2%) | 0 |
| Keratic precipitates | 0 | 1 (0.2%) | 0 |
| Keratouveitis | 0 | 1 (0.2%) | 0 |
| **Endophthalmitis events** | 2 (0.3%) | 4 (0.6%) | 1 (0.2%) |
| **Retinal vasculitis events** | 0 | 0 | 0 |
| **Retinal occlusive events** | | | |
| Retinal vein occlusion | 1 (0.2%) | 4 (0.6%) | 0 |
| Retinal artery occlusion | 1 (0.2%) | 2 (0.3%) | 2 (0.3%) |
| Retinal artery embolism | 0 | 0 | 1 (0.2%) |
| **Serious non-ocular AEs** | 175 (27.8%) | 161 (25.5%) | 173 (27.7%) |
| **APTC events[e]** | 34 (5.4%) | 30 (4.7%) | 32 (5.1%) |

Results are presented for the pooled YOSEMITE/RHINE safety-evaluable population. [a]Percentages are based on n values in the column headings; multiple occurrences of the same AE in an individual are counted only once. [b]Ocular AEs in the study eye only are presented. [c]Ocular AEs of special interest were defined as events associated with severe intraocular inflammation, events requiring surgical or medical intervention to prevent permanent loss of sight or events associated with BCVA loss of ≥ 30 letters for > 1 hour. [d]Excluding endophthalmitis. [e]APTC events were adjudicated by an external independent committee; all other events were investigator reported. Includes AEs with onset from the first dose of study drug through study end.

### Robust Vision Gains and CST Reductions With Faricimab at Year 1 Were Maintained Through Year 2

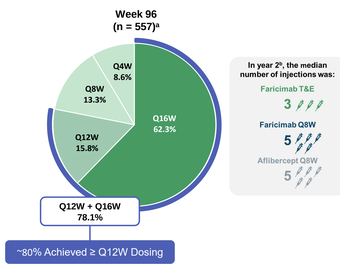
YOSEMITE/RHINE Pooled




* *P* values are nominal and not adjusted for multiplicity; no formal statistical conclusion should be made based on the *P* values. Clinical significance has not been established and conclusions regarding treatment effect cannot be drawn.
[a]Adjusted mean change from baseline at 2 years, averaged over weeks 92, 96 and 100. Results are based on a mixed model for repeated measures analysis, adjusted for treatment group, visit, visit-by-treatment group interaction, baseline CST (continuous) as applicable, baseline BCVA (< 64 vs ≥ 64 ETDRS letters), prior intravitreal anti-VEGF therapy (yes vs no), region (US and Canada, Asia and the rest of the world) and study (YOSEMITE vs RHINE). 95% CI error bars are shown. BCVA, best-corrected visual acuity; CST, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study; Q8W, every 8 weeks; T&E, treat-and-extend; VEGF, vascular endothelial growth factor.

### In Year 2, Faricimab Up to Q16W Achieved Durable Vision Gains With Fewer Injections vs Aflibercept in Patients With DMO

YOSEMITE/RHINE Pooled




~80% Achieved ≥ Q12W Dosing

[a] Proportion of patients in the pooled faricimab T&E arms on Q4W, Q8W, Q12W or Q16W dosing at week 96, among those who had not discontinued the study at the week 96 visit; results are presented for the pooled YOSEMITE/RHINE safety-evaluable population (faricimab Q8W, n = 630; faricimab T&E, n = 632; aflibercept Q8W, n = 625). [b] Weeks 40–96. DMO, diabetic macular oedema; Q4W, every 4 weeks; Q8W, every 8 weeks; Q12W, every 12 weeks; Q16W, every 16 weeks; T&E, treat-and-extend.

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## References

1. NICE. Technology Appraisal Guidance T799. 2022
2. Gale R et al. Intravitreal faricimab for DMO: Expert panel consensus. OTE, May 2023
3. Diabetic Retinopathy Clinical Research N, Wells JA et al.N Engl J Med. 2015;372:1193-1203.
4. Schmidt-Erfurth U et al. Ophthalmologica. 2017;237(4):185-222.
5. Vabysmo 120 mg/mL solution for injection [Summary of Product Characteristics]; Roche Products Limited, UK, December 2022.
6. Amoaku WM et al. Eye (Lond). 2020;34(Suppl 1):1-51.
7. Downey L et al. BMJ Open Ophthalmol. 2021;6(1):e000696
8. Wykoff CC et al; YOSEMITE and RHINE Investigators. Lancet. 2022;399(10326):741-755.
9. Joussen AM et al. Eye (Lond). 2021;35(5):1305-1316

## Financial Disclosures

- All authors except RP and NJ, who are employees of Roche Products Ltd, received honoraria from Roche Products Ltd for their contributions as members of the expert roundtable. All authors contributed to development and approval of the manuscript.

## Study and Product Disclosures

- Faricimab is approved for the treatment of neovascular age-related macular degeneration and diabetic macular oedema in multiple countries worldwide and is not currently approved for use outside these indications
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