Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2499

# faricimab 120mg/mL solution for injection (Vabysmo®)

## Roche Products Limited

07 October 2022

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

**ADVICE**: following a full submission

**faricimab (Vabysmo®)** is accepted for restricted use within NHSScotland.

**Indication under review:** For the treatment of adult patients with visual impairment due to diabetic macular oedema (DMO).

**SMC restriction:** treatment of visual impairment due to DMO in adults with best corrected visual acuity (BCVA) of 75 Early Treatment Diabetic Retinopathy Study (ETDRS) letters or less at baseline.

In two phase III studies faricimab was non-inferior to an anti-vascular endothelial growth factor treatment for change in BCVA from baseline at 1 year.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

**Chairman**
**Scottish Medicines Consortium**

## Indication

For the treatment of adult patients with visual impairment due to diabetic macular oedema (DMO).[1]

## Dosing Information

The recommended dose is 6mg (0.05 mL solution) administered by intravitreal injection every 4 weeks for the first 4 doses. Each vial should only be used for the treatment of a single eye.

Thereafter, treatment may be individualised using a treat-and-extend approach following an assessment of the individual patient's anatomic and visual outcomes. The dosing interval may be extended from every 4 to every 16 weeks, with extensions in increments of up to 4 weeks, based on the physician's judgement of the individual patient's anatomic and/or visual outcomes. If anatomic and/or visual outcomes change, the treatment interval should be adjusted accordingly, and interval reductions of up to 8 weeks may be implemented if deemed necessary.

Faricimab is intended for long-term treatment. If visual and/or anatomic outcomes indicate that the patient is not benefitting from continued treatment, faricimab should be discontinued.

Faricimab must be administered by a qualified healthcare professional trained in intravitreal injections.[1]

## Product availability date

31 July 2022

# Summary of evidence on comparative efficacy

Faricimab is a bispecific immunoglobulin G1 antibody that through inhibition of two distinct pathways, angiopoietin-2 and vascular endothelial growth factor A (VEGF-A) reduces vascular permeability and inflammation, inhibits pathological angiogenesis and restores vascular stability.[1]

Evidence to support the efficacy and safety of faricimab for the indication under review is from two randomised double-blind phase III studies, YOSEMITE and RHINE. Both studies were identical in design and recruited adult patients with macular oedema secondary to diabetes mellitus (type 1 or 2) with a central subfield thickness (CST) ≥325 micrometres and best-corrected visual acuity (BCVA) of 73 to 25 Early Treatment Diabetic Retinopathy Study (ETDRS) letters (approximate Snellen equivalent 20/40 to 20/320). One eye per patient was permitted for study enrolment, if both eyes were eligible the eye with worse BCVA at screening was selected. Study eyes could be anti-VEGF treatment-naïve or previously treated (provided that the last treatment was 3 months

or more before the day 1 study visit). Previously treated study eyes were limited to 25% of the total enrolment.[2]

In both studies, patients were randomised equally to receive via intravitreal injection:

- faricimab 6mg every 4 weeks up to week 20 (six injections), then fixed dosing every 8 weeks up to week 96.
- faricimab 6mg every 4 weeks up to week 12 (four injections), then per personalised treatment interval (PTI) with adjustable dosing up to every 16 weeks until week 96.
- aflibercept 2mg every 4 weeks up to week 16 (five injections), then fixed dosing every 8 weeks up to week 96.

The PTI dosing regimen was based on a treat-and-extend approach where patients received faricimab 6mg every 4 weeks until they first reached a CST <325 micrometres at or after week 12. Once achieved, treatment intervals were extended to every 8 weeks and then could be maintained, extended by 4 weeks (up to every 16 weeks), or reduced by 4 weeks or 8 weeks (as low as every 4 weeks) based on pre-specified CST and BCVA criteria at active dosing visits. Randomisation was stratified by baseline BCVA (<64 or ≥64 ETDRS letters), previous intravitreal anti-VEGF therapy (yes or no), and region (USA and Canada or Asia and rest of the world combined).[2]

The primary outcome was change in BCVA (as measured on the ETDRS chart at a starting distance of 4 metres) from baseline at 1 year, averaged over weeks 48, 52, and 56. The outcome was averaged over three time points to account for BCVA variability over time and differences in time from last treatment between patients. Efficacy analyses were performed in the intention-to-treat (ITT) population, which included all patients who underwent randomisation. A hierarchical statistical testing strategy was applied in the study with no formal testing of outcomes after the first non-significant outcome in the hierarchy. The primary outcome was tested in the following prioritised order: non-inferiority of faricimab versus aflibercept every 8 weeks in the ITT population, superiority of faricimab versus aflibercept every 8 weeks in the treatment-naive population, superiority of faricimab versus aflibercept every 8 weeks in the ITT population.[2]

In YOSEMITE and RHINE, both faricimab treatment groups demonstrated non-inferiority to aflibercept for the primary outcome of mean change from baseline in BCVA at 1 year in the ITT population. This was because the lower bound of the 97.5% confidence intervals for the adjusted mean difference between both the faricimab groups and aflibercept group was greater than the non-inferiority margin of -4 letters. Results from the primary and selected secondary outcomes are detailed in table 1.[1, 2]

**Table 1: Primary and selected secondary outcomes from YOSEMITE and RHINE in the ITT population[1, 2]**

| | YOSEMITE | | | RHINE | | |
|---|---|---|---|---|---|---|
| | **Faricimab 8 weekly n=315** | **Faricimab PTI n=313** | **Aflibercept 8 weekly n=312** | **Faricimab 8 weekly n=317** | **Faricimab PTI n=319** | **Aflibercept 8 weekly n=315** |
| **Primary outcome: Change from baseline in BCVA at 1 year** | | | | | | |
| Adjusted mean change in BCVA* | 10.7 | 11.6 | 10.9 | 11.8 | 10.8 | 10.3 |
| LS mean difference versus aflibercept, (97.5% CI) | -0.2 (-2.0 to 1.6) | 0.7 (-1.1 to 2.5) | - | 1.5 (-0.1 to 3.2) | 0.5 (-1.1 to 2.1) | - |
| **Selected secondary outcomes measured at 1 year** | | | | | | |
| Patients with a ≥2-step improvement on the ETDRS DRSS | 46% | 42% | 36% | 44% | 44% | 47% |
| Patients gaining ≥15 letters in BCVA | 29% | 36% | 32% | 34% | 28% | 30% |
| Change from baseline in CST, microns** | -206.6 | -196.5 | -170.3 | -195.8 | -187.6 | -170.1 |

BCVA= best corrected visual acuity; CI=confidence interval; CST= central subfield thickness; DRSS= Diabetic Retinopathy Severity Scale; ETDRS= Early Treatment Diabetic Retinopathy Study; LS=least square *measured by ETDRS letter score from baseline, ** measured in patients with evaluable colour fundus photograph images at baseline and week 52.

In the treatment-naïve population, faricimab (8 weekly or PTI) was not superior to aflibercept for the primary outcome, therefore subsequent testing of superiority in the ITT population was not conducted.[2]

At year 2 (averaged over week 92, 96 and 100) the mean change in BCVA in the faricimab 8 weekly, faricimab PTI and aflibercept groups in YOSEMITE (10.7, 10.7, 11.4 letters in each group respectively) and RHINE (10.9, 10.1, 9.4 letters in each group respectively) and the proportion of patients with a ≥2 step improvement on the ETDRS-DRSS (51%, 43% and 42% in YOSEMITE and 54%, 44%, 44% in RHINE for each group respectively) were generally maintained.[1]

The proportion of patients in the faricimab PTI group that were on a 16 or 12 weekly dosing interval at 1 year was 74% and 71% in YOSEMITE and RHINE respectively (53% and 51% on 16 weekly dosing; 21% and 20% on 12 weekly dosing). The proportion on an extended dosing interval

was similar at week 96, with 78% of patients in the faricimab PTI group in both studies on either 16 or 12 weekly dosing (60% and 64% on 16 weekly dosing; 18% and 14% on 12 weekly dosing). In YOSEMITE and RHINE respectively, 13% and 18% received >15 injections in the faricimab PTI arm at week 96.[1, 2]

Health Related Quality of Life (HRQoL) was assessed using the National Eye Institute Visual Functioning Questionnaire-25 (NEI VFQ-25). The NEI VFQ-25 captures a patient's perception of vision-related functioning and vision-related quality of life. The composite score and subscale scores range from 0 to 100, with higher scores indicating better vision-related functioning. In both studies, similar mean improvements in the NEI VFQ-25 composite score in all groups were observed at week 52 and week 100.[3-6]

The submitting company performed a Bayesian network meta-analysis (NMA) to assess the efficacy and safety of faricimab PTI in adult patients with DMO compared with aflibercept (dosing regimens included 4 weekly, 8 weekly and PRN) and ranibizumab (dosing regimens included 4 weekly, PRN and treat-and-extend). Twenty-six studies were included in the NMA base-case analysis and outcomes included mean change in BCVA score, mean change in CST and mean number of injections, ocular adverse events and all-cause discontinuation measured from baseline to 1 year. Overall, the results of the NMA indicated comparable efficacy between faricimab PTI and aflibercept or ranibizumab for the outcomes measured and possibly favourable improvements for some outcomes for particular dosing intervals.

*Other data were also assessed but remain confidential.**

## Summary of evidence on comparative safety

In the YOSEMITE study up to week 56, ocular adverse events (AE) were reported by 31% (98/313) of patients in the faricimab 8 weekly group, 34% (106/313) in the faricimab PTI group and 33% (102/311) in the aflibercept group. The proportion of patients in each group with a treatment-related ocular AE was 3.5%, 2.6% and 1.6% respectively and these were considered serious in 0%, 1.3% and 0%. Non-ocular AEs were reported by 65%, 67% and 65% in each treatment group. The most frequently reported ocular AEs of any grade with an incidence >2% in the faricimab 8 weekly group, faricimab PTI group and aflibercept group were: conjunctival haemorrhage (6.4%, 7.0% and 6.1%), vitreous floaters (4.8%, 1.9% and 0.6%), cataract (4.5%, 3.5% and 5.5%), vitreous detachment (3.2%, 3.5% and 2.9%), intraocular pressure increased (3.2%, 1.6% and 1.6%), eye pain (2.6%, 2.2% and 2.9%) and dry eye (2.6%, 1.0% and 1.3%).[2]

In the RHINE study up to week 56, ocular AEs were reported by 43% (137/317) of patients in the faricimab 8 weekly group, 37% (119/319) in the faricimab PTI group and 36% (113/314) in the aflibercept group. The proportion of patients in each group with a treatment-related ocular AE was 2.5%, 2.5% and 4.5% respectively and these were considered serious in 0%, 0.3% and 0%. Non-ocular AEs were reported by 60%, 55% and 60% in each treatment group. The most frequently reported ocular AEs of any grade with an incidence >2% in the faricimab 8 weekly

group, faricimab PTI group and aflibercept group were: conjunctival haemorrhage (8.2%, 5.0% and 6.1%), cataract (5.7%, 4.7% and 4.1%), vitreous floaters (4.7%, 2.2% and 2.5%), vitreous detachment (4.1%, 2.2% and 3.5%), intraocular pressure increased (4.1%, 2.8% and 2.5%), eye pain (1.3%, 2.5% and 3.2%) and dry eye (4.4%, 3.4% and 2.2%). Refer to the Summary of product characteristics (SPC) for further safety information.[1, 2]

## Summary of clinical effectiveness issues

Diabetic macular oedema has become a major cause of vision loss worldwide due to the increased incidence of diabetes. It is characterised by increased permeability of the retinal vasculature and fluid accumulation in the macula that causes blurring and a distortion of central vision reflected by a reduction in BCVA. Treatment options for DMO include anti-VEGF therapy, corticosteroids and laser photocoagulation. Standard first-line treatment is with intravitreal anti-VEGF therapy. Ranibizumab and aflibercept are anti-VEGF options that have been accepted by SMC for the treatment of visual impairment due to DMO and have been restricted for use in patients with BCVA 75 Early Treatment Diabetic Retinopathy Study (ETDRS) letters or less at baseline (SMC711/11 and SMC1003/14). Brolucizumab is another anti-VEGF therapy that has recently been licensed for the treatment of visual impairment due to DMO.[2, 7, 8]

In YOSEMITE and RHINE, faricimab administered every 8 weeks or using a PTI approach was non-inferior to aflibercept every 8 weeks for the mean change in BCVA from baseline to 1 year in patients with DMO. The treatment effect was generally maintained at year 2. A 16-week dosing interval was achieved by 53% and 51% of patients in the faricimab PTI group in each study at year 1 and by 60% and 64% at year 2.[1, 2]

There were some limitations with the evidence presented. In YOSEMITE and RHINE, following the initial 5 doses, aflibercept was administered every 8 weeks as recommended in the SPC. However, the SPC states that after the first 12 months, treatment may be extended, usually in 2-week intervals based on clinical judgement and anatomic outcomes in a treat-and-extend dosing regimen.[9] This was not permitted within either study protocol, therefore the dosing interval for aflibercept beyond year 1 may not reflect clinical practice. The main publication noted that YOSEMITE and RHINE were not designed to assess the head-to-head durability of faricimab versus aflibercept.[2] Long term evidence beyond 2 years is limited as data from YOSEMITE and RHINE are available for up to 96 weeks only. RHONE-X is an ongoing two-year open-label extension which includes patients who completed YOSEMITE and RHINE and is expected to complete in August 2023. There is also no evidence for bilateral treatment. Secondary outcomes were not controlled for multiplicity and are therefore considered descriptive only.[2, 10]

It is uncertain if the PTI approach used for faricimab in YOSEMITE and RHINE is reflective of the treat-and-extend approach used in Scotland which may affect the generalisability of study results to clinical practice. Most patients recruited to YOSEMITE and RHINE were anti-VEGF treatment naïve and therefore evidence in patients who have previously received anti-VEGF treatment (23%

in YOSEMITE and 20% in RHINE) is limited.[2] Subgroup analysis based on prior anti-VEGF treatment indicated that results were generally consistent with the overall population for the primary outcome at 1 year.[3, 4]

The submitting company consider that faricimab will be used as an alternative first line option to ranibizumab and aflibercept however, these are accepted for restricted for use in NHSScotland for treatment of visual impairment due to DMO in adults with BCVA of 75 ETDRS letters or less at baseline. YOSEMITE and RHINE provide direct evidence comparing faricimab and aflibercept, however ranibizumab is an alternative anti-VEGF therapy that may be used in clinical practice. In the absence of direct evidence the submitting company presented NMA comparing faricimab with aflibercept and ranibizumab. The NMA were associated with a number of limitations: the inclusion of comparators that are not used in NHSScotland, ranibizumab 0.3mg and 0.5mg doses were assumed equivalent based on limited data, there was clinical and methodological heterogeneity between studies including differences in the mean or range of BCVA in patients and differences in loading dose regimens before entering the maintenance dosing phase of treatment. The credible intervals around the results for some outcomes were wide indicating increased uncertainty. Despite these limitations, a conclusion of similar efficacy seems reasonable.

*Other data were also assessed but remain confidential.**

## Summary of comparative health economic evidence

The company submitted a cost-minimisation analysis for the comparison of faricimab, aflibercept and ranibizumab for the treatment of adult patients with visual impairment due to DMO. The analysis adopted a 25-year time horizon.

The economic analysis had 3 health states: on treatment (study eye or both eyes), off treatment and dead. The cycle length was 4 weeks.

Treatment included a loading phase (4 injections for faricimab and 5 for aflibercept and ranibizumab), followed by a pre-defined personalised treatment interval (PTI) regimen. The treat and extend (T&E) regimen was assumed in the faricimab year up to year 2 in the model, followed by the pro re nata (PRN) or “as needed” regimen, whereas the PRN was assumed in the comparator arms for the duration of treatment.

Equivalent efficacy was assumed in the economic model and only number of injections, administration visits and monitoring visits being modelled separately across treatments. Data for faricimab came from the 2 relevant clinical studies (YOSEMITE and RHINE) up to 2 years, followed by assumptions, whereas data for the comparators came from the network meta-analysis in year 1 and Protocol T study (comparison of aflibercept, ranibizumab and bevacizumab) thereafter.[2, 11 2, 11] A minimum of four visits (administration and monitoring) annually were assumed from year 3 onwards. Equivalent discontinuation rates were included in the analysis annually as observed in the relevant faricimab studies. A maximum treatment duration of 5 years was assumed for 85% of patients with the remaining 15% discontinuing at 4.1% annual rate. Additionally, at baseline 46.5% of patients were modelled to have bilateral disease, increasing at a 10% annual rate for people

who are alive and still receiving treatment in their first eye. Due to the assumption of difference in treatment regimens, overall lower number of administration and monitoring visits were lower for faricimab compared with aflibercept and ranibizumab in the company's base-case analysis. No monitoring visits were assumed in the faricimab arm for the duration of the T&E regimen.

General population all-cause mortality was also included in the model, adjusted to reflect the YOSEMITE and RHINE patient population, in terms of age- and gender-specific mortality rates. Mortality was further adjusted by applying a diabetes specific hazard for the entire population as well as health state mortality risks from being blind and visually impaired.

Aside from medicine acquisition and administration costs, other costs included in the analysis were those of optical coherence tomography (OCT) at diagnosis and at every administration and monitoring visit, cost of a consultant-led outpatient appointment and staff time. To account for fellow eye involvement, a cost multiplier of 2.0 was applied to drug costs and 1.877 to administration and monitoring costs.

A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a simple discount was offered on the list price for faricimab.

A PAS is also in place for aflibercept and ranibizumab. The results presented do not take account of the PAS for faricimab, aflibercept and ranibizumab but these were considered in the results used for decision-making. SMC is unable to present the results provided by the company which used an estimate of the PAS price for aflibercept and ranibizumab due to commercial confidentiality and competition law issues.

**Table 2: Base case results (list price for all medicines)**

| Cost | Faricimab | Aflibercept | Ranibizumab |
|---|---|---|---|
| **Drug cost** | £26,897 | £28,633 | £19,329 |
| **Administration cost** | £8,138 | £9,103 | £9,097 |
| **Monitoring cost** | £2,024 | £4,297 | £4,167 |
| **Diagnostic cost** | £194 | £194 | £194 |
| **Mean total cost** | £37,272 | £42,227 | £32,787 |
| **Incremental cost faricimab vs comparator** | - | -£4,955 | £4,485 |

A range of scenario analyses are presented in table 3.

**Table 3: Scenario analyses (list price for all medicines)**

| | Scenario | Incremental cost vs aflibercept | Incremental cost vs ranibizumab |
|---|---|---|---|
| 0 | Base-case | -£4,955 | £4,485 |
| 1 | Equivalent number of injections after loading phase | -£3,291 | £4,852 |
| 2 | Equivalent number of monitoring visits | -£2,714 | £6,599 |
| 3 | Combine scenarios 1 and 2 | -£622 | £7,192 |

| | | | |
|---|---|---|---|
| 4 | Equivalent number of injections and monitoring visits for faricimab and comparators (8 in year 1, 4 in year 2 and 2 in year 3+). | £1,314 | £9,128 |

Key limitations with the analysis were:

- There is uncertainty around the appropriateness of the assumption of difference in frequency of administration between faricimab and comparators. The company-provided network meta-analysis found no statistically significant differences in injection frequencies between faricimab T&E and ranibizumab or aflibercept PRN treatment regimens. However, a clinical expert consulted by SMC noted their expectation for faricimab to be administered less frequently in at least 50% of patients. The impact of assuming equivalent number of injections post loading phase on cost-minimisation results are presented in table 3 scenario 1.

- The assumption of no monitoring visits required during a T&E regimen (assumed for faricimab only) may also not be appropriate. A clinical expert consulted by SMC, stated that separate monitoring visits may still be required alongside a T&E regimen and this is supported by clinical guidelines (guidelines and protocols sections below). The impact of assuming equivalent number of monitoring visits post loading phase on cost minimisation results are presented in table 3 scenario 2. A combination scenario (table 3, scenario 3) as well as a scenario where equivalence in all clinical model parameters is assumed (table 3, scenario 4) are also presented.

Despite the limitations, the economic case has been demonstrated.

## Summary of patient and carer involvement

The following information reflects the views of the specified Patient Group.

- We received a patient group submission from the Macular Society, which is a registered charity.

- The Macular Society has received 3.5% pharmaceutical company funding in the past two years, including from the submitting company.

- Diabetic macular oedema (DMO) is a complication of diabetes that can lead to irreversible sight loss. It is one of the most common causes of sight loss in the working age group. Loss of central vision through DMO can be very frustrating and can greatly affect everyday life as well as financial impact due to changes in employment and ability to drive. Vision loss can make daily tasks more difficult, including tasks needed to monitor and manage diabetes. There is a significant burden on family and carers supporting a patient with DMO as the emotional and practical impacts of the condition mean the patient will often rely on them to provide additional support.

- Some patients do not respond well to currently available treatments. Generally, patients who responded to a survey conducted by the patient group felt less able to manage their eye health and DMO compared with their diabetes.

- Patients consider faricimab to be an innovative treatment which offers more hope in addition to treatments currently available as it is dual action, targeting both angiopoietin (Ang-2) and vascular endothelial growth factor (VEGF).

## Additional information: guidelines and protocols

The European Society of Retina Specialists (EURETINA) published Guidelines for the Management of Diabetic Macular Oedema in 2017.[8] These guidelines recommend anti-VEGF therapy as the first-line treatment with steroids recommended in the management of chronically persistent DMO. The agents that are recommended by the EURETINA include aflibercept, ranibizumab and off-label bevacizumab. Laser treatment (including laser photocoagulation) is no longer standard of care.

Specific recommendations for anti-VEGF treatments are as follows[8] –

- Aflibercept is the preferred treatment in DMO eyes with baseline BCVA below 69 letters, as it shows superiority to bevacizumab over 2 years and over ranibizumab in the first year of treatment. Dosing options include a course of loading injections at 4-weekly intervals followed by a regimen of fixed bimonthly injections or a PRN regimen with monthly monitoring only.
- Ranibizumab can be used equivalent to other available anti-VEGF agents for patients with a baseline BCVA letter score of 69 letters and above. For patients with poorer baseline visual acuity ranibizumab will most likely result in the same visual acuity results after 2 years of treatment as aflibercept, but the effect will be reached slightly slower. Therefore, treatment shall be initiated with aflibercept, if available, in these patients. Treatment with ranibizumab should be initiated early on with monthly injections. If visual acuity improves and/or central retinal thickness (CRT) decreases, monthly injections must be continued until outcomes remain stable with appropriate extension to the interval of injections and monitoring visits. If no more functional or anatomical benefit occurs, the treatment must be stopped, and extended monitoring intervals can be evaluated for each patient individually.
- Aflibercept, ranibizumab and bevacizumab (used off-label) are equivalent in improving vision in eyes with a baseline BCVA letter score of 69 or more.

## Additional information: comparators

Aflibercept and ranibizumab

## Additional information: list price of medicine under review

| Medicine | Dose Regimen | Cost per year (£) |
|---|---|---|
| Faricimab | 6mg by intravitreal injection every 4 weeks for the first 4 doses. Thereafter, The dosing interval may be extended from every 4 to every 16 weeks, with extensions in increments of up to 4 weeks, based on the physician's judgement of the individual patient's anatomic and/or visual outcomes. | Year 1: 5,999 to 11,141<br><br>Subsequent years: 2,571 to 11,141 |

*Costs from Dictionary of Medicines and Devices Browser on 07/08/22. Costs do not take patient access schemes into consideration.*

## Additional information: budget impact

The submitting company estimated there would be 7,540 patients eligible for treatment with faricimab in year 1 rising to 7,639 in year 5. The estimated uptake rate was 1.0% in year 1 and 27.0% in year 5. This resulted in 75 patients estimated to receive treatment in year 1 rising to 2,063 patients in year 5.

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines.

*Other data were also assessed but remain confidential.**

**References**


1. Roche Products Limited. Faricimab solution for injection (Vabysmo®) Summary of product characteristics. Electronic Medicines Compendium https://www.medicines.org.uk/emc/product/13741/smpc#gref Last updated: 18 May 2022.
2. Wykoff CC, Abreu F, Adamis AP, Basu K, Eichenbaum DA, Haskova Z*, et al.* Efficacy, durability, and safety of intravitreal faricimab with extended dosing up to every 16 weeks in patients with diabetic macular oedema (YOSEMITE and RHINE): two randomised, double-masked, phase 3 trials. Lancet. 2022;399(10326):741-55. Epub 2022/01/28.
3. F. Hoffmann-La Roche Ltd. Clinical study report (CSR). Primary CSR Study GR40349 (YOSEMITE) 2021: Report No. 1102956.
4. F. Hoffmann-La Roche Ltd. Clinical study report (CSR). Primary CSR Study GR40398 (RHINE) 2021: Report No. 1102957.
5. F. Hoffman-La Roche Ltd. Clinical study report (CSR). FInal CSR Study GR40349 (YOSEMITE) 2022: Report No. 1111791.
6. F. Hoffman-La Roche Ltd. Clinical study report (CSR). Update CSR Study GR40398 (RHINE) 2022: Report No. 1112142.
7. Novartis Pharmaceuticals UK Ltd. Brolucizumab 120 mg/ml solution for injection in pre-filled syringe (Beovu®) Summary of product characteristics. Electronic Medicines Compendium https://www.medicines.org.uk/emc/product/11145/smpc#PHARMACOLOGICAL_PROPS Last updated 5 May 2022.
8. U. Schmidt-Erfurth et al. Guidelines for the Management of Diabetic Macular Edema by the European Society of Retina Specialists (EURETINA). Ophthalmologica 2017;237:185–222.
9. Bayer plc. Aflibercept solution for injection in a vial (Eylea®) Summary of Product Characteristics. Electronic Medicines Compendium https://www.medicines.org.uk/emc/product/2879/smpc#gref Last updated: 18 August 2021. [cited.
10. ClinicalTrials.gov. A Study to Evaluate the Long-Term Safety and Tolerability of Faricimab in Participants With Diabetic Macular Edema (Rhone-X) NCT04432831. Last updated: 8 June 2022. Available at: https://clinicaltrials.gov/ct2/show/NCT04432831?term=rhone-x&draw=2&rank=1.
11. Wells JA, Glassman AR, Ayala AR, Jampol LM, Aiello LP, Antoszyk AN*, et al.* Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema. The New England journal of medicine. 2015;372(13):1193-203. Epub 2015/02/19.


This assessment is based on data submitted by the applicant company up to and including 15 September 2022.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

**Advice context:**

*No part of this advice may be used without the whole of the advice being quoted in full.*

*This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.*