NCPE Assessment

Technical Summary

Faricimab (Vabysmo®)

22061

30 June 2025

Applicant: Roche Products Ireland Ltd

Faricimab for the treatment of adults with diabetic macular oedema.

NCPE
National Centre for Pharmacoeconomics, Ireland

The National Centre for Pharmacoeconomics (NCPE) has issued a recommendation regarding the cost-effectiveness of faricimab (Vabysmo®).

Following assessment of the Applicant's submission, the NCPE recommends that faricimab (Vabysmo®) not be considered for reimbursement unless cost-effectiveness can be improved relative to existing treatments.

The Health Service Executive (HSE) asked the NCPE to carry out an evaluation of the Applicant's (Roche Products Ireland Ltd) Health Technology Assessment of faricimab (Vabysmo®). The NCPE uses a decision framework to systematically assess whether a technology is cost-effective. This includes comparative clinical effectiveness and health-related quality of life benefits, which the new treatment may provide and whether the cost requested by the pharmaceutical company is justified.

Following the recommendation from the NCPE, the HSE examines all the evidence which may be relevant for the decision; the final decision on reimbursement is made by the HSE. In the case of cancer drugs the NCPE recommendation is also considered by the National Cancer Control Programme (NCCP) Technology Review Group.

About the National Centre for Pharmacoeconomics

The NCPE are a team of clinicians, pharmacists, pharmacologists and statisticians who evaluate the benefit and costs of medical technologies and provide advice to the HSE. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. Our aim is to provide impartial advice to help decision makers provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has a responsibility for commissioning or providing healthcare, public health or social care services.

Summary

In June 2024, Roche Products Ireland Ltd submitted a dossier which compared faricimab to current standard of care anti-VEGF [vascular endothelial growth factor] therapies in the treatment of adults with diabetic macular oedema (DMO). Estimated prevalence rates from the literature suggest a global prevalence rate of DMO of 7.5% in the population with diabetes, resulting in a potential DMO prevalent population of 17,791 in Ireland. Roche Products Ireland Ltd are seeking reimbursement of faricimab in the hospital setting.

Faricimab is a humanized bispecific immunoglobulin G1 antibody that acts through inhibition of two distinct pathways by neutralisation of both angiopoietin-2 and vascular endothelial growth factor A, reducing vascular permeability and inflammation. The recommended dose of faricimab is 6mg administered by intravitreal (IVT) injection once every four weeks (q.4.w) for the first three loading doses. Thereafter, an assessment of disease activity, based on anatomic and or visual outcomes, is recommended so that maintenance doses can be individualised to either once every eight weeks (q.8.w), once every twelve weeks (q.12.w) or once every sixteen weeks (q.16.w). Faricimab is intended for long-term as per the Summary of Product Characteristics (SmPC).

Three anti-VEGF therapies are licensed by the EMA for the treatment of DMO; all are given by intravitreal injection. These are aflibercept (Eylea®), brolucizumab (Beovu®) and ranibizumab (Lucentis®). Bevacizumab ection is available for off-label use in the management of DMO. No anti-VEGF intravitreal therapies (IVTs) are centrally reimbursed by the HSE. Clinician feedback confirmed that bevacizumab is used first line in clinical practice (for both DMO and wet age-related macular degeneration). Aflibercept and ranibizumab are also prescribed as an alternative first-line therapy in some treatment centres in Ireland. Both aflibercept and ranibizumab are also available as a second-line therapy in Ireland. Brolucizumab is not used in the Irish treatment setting as per clinical opinion and therefore has not been included as a comparator. The Review Group consider this to be appropriate. Clinical opinion obtained by the Review Group reported that the maintenance treatment, with anti-VEGF IVTs in DMO predominantly follows either an As Required (PRN) approach or a Treat and Extend (T&E) approach in clinical practice in Ireland. The clinical trial programme

investigating faricimab adopted a personalised treatment schedule arm which allowed for a change in the frequency of injection from 1 month to 4 months, depending on the activity of the disease. The Applicant indicated that anti-VEGF IVT comparators primarily followed a PRN dosing schedule, rather than a T&E approach.

The Applicant anticipates that faricimab will be used as a second-line treatment after first-line anti-VEGF (assumed to be bevacizumab) treatment. However, the Review Group note that the licensed indication for faricimab does not restrict its use to any line of therapy in DMO. The clinical trial evidence supporting product registration (the YOSEMITE and RHINE trials) included both treatment experienced and treatment-naïve participants with DMO, which are used to inform the health-economic model. The Review Group do not consider the Applicant's assumption that faricimab will be used as a second-line treatment to be appropriate. This aligns with clinical opinion obtained by the Review Group who report that, should faricimab be reimbursed, that it will be used in the first line setting (displacing bevacizumab), also as a second line agent in non and partial responders to first line bevacizumab and also as a second line agent in patients that currently require frequent injections with bevacizumab to achieve disease stability. It is possible therefore that faricimab would also be used in the first-line setting, as per its product licence, unless gatekeeping measures are implemented by the HSE.

1. Comparative effectiveness of faricimab

The efficacy and safety of faricimab was assessed in two identically designed, pivotal, phase III, randomised, double-blinded, non-inferiority trials (YOSEMITE n=940 and RHINE n=951). These trials were designed to evaluate the safety and efficacy of faricimab versus aflibercept in adults with DMO. Participants were randomised to IVT faricimab 6mg once every 8 weeks (q.8.w) arm, faricimab 6mg per personalised treatment interval (PTI) arm, or aflibercept once q.8.w arm. In the faricimab once q.8.w. arm, patients received faricimab IVT injections once every four weeks (q.4.w) to Week 20 followed by once q.8.w to Week 96. In the PTI arm, patients received faricimab IVT injections once q.4.w to Week 12, then dosing intervals were extended, maintained, or reduced thereafter (from once q.4.w to once every 16 weeks (q.16.w) based on disease activity assessed at each dosing visit). In the aflibercept once q.8.w arm, aflibercept 2mg was administered once q.4.w up to Week 8, followed by a

fixed-dosing interval of once q.8.w up to Week 96. Efficacy analyses were performed in the intention-to-treat (ITT) population, which included all participants who underwent randomisation, with sensitivity analysis in the treatment naïve (TN) population. Approximately 22% of participants recruited to YOSEMITE and RHINE had been previously treated with an anti-VEGF; this was equivalent across arms. Both trials met their primary efficacy endpoint, demonstrating that faricimab (administered at once q.8.w or PTI dosing) was noninferior to aflibercept once q.8.w in the change in Best Corrected Visual Acuity (BCVA) from baseline outcome averaged over Weeks 48, 52, and 56 (Year 1 time point) . A further follow up with two years' data was also included in the Applicant's submission which assessed the primary endpoint over an average of Weeks 92, 96 and 100 (Year 2 time point) . The efficacy results were consistent across Year 1 and Year 2 time points. Primary and secondary efficacy results in the pooled TN population were generally consistent with the results in the overall populations across both Year 1 and 2 timepoints. A once q.16.w interval was achieved by 52% of participants treated with faricimab (PTI arm) pooled across both trials at Year 1 and by 62% at Year 2. The Review Group consider the following key limitations; aflibercept was given at a fixed-dosing interval in the maintenance phase which does not align with the T&E protocol commonly used in clinical practice in Ireland. It also contrasts with the SmPC for aflibercept which allows for longer treatment intervals using at T&E approach, thus limiting the generalisability of the trials' results.

The comparative effectiveness analysis included a network meta-analysis (NMA) in a Bayesian framework to inform the comparison between faricimab in adult patients with DMO compared with aflibercept, ranibizumab, and bevacizumab administered according to all administration protocols; T&E, PRN and fixed-dosing interval. Twenty-nine studies were included in the NMA. The Review Group note the substantial between-study heterogeneity in the studies deemed eligible for inclusion in the NMA. This may result in bias and imprecision in the resulting treatment effect estimates. Although aflibercept, ranibizumab and bevacizumab are administered according to T&E regimens in Irish clinical practice, outcome data for these regimens were mostly unavailable. Results of the Applicant's NMA suggest that faricimab (T&E) had comparable efficacy in mean change to BCVA from baseline to 12 and 24 months compared with relevant comparator anti-VEGF IVTs administered according to PRN protocols.The Applicant's claim that faricimab will lead to a reduced

injection frequency has not been established by this analysis. The numerical reduction in injections given may be at least partly explained by chance effects and differences in T&E and PRN protocols between studies. Therefore, it cannot be concluded that the reduced injection frequency represents a true causal effect of faricimab treatment.

2. Safety of faricimab

Pooled safety data from pivotal trials (YOSEMITE and RHONE) indicate that faricimab was well tolerated with an acceptable safety profile comparable with aflibercept up to Week 112. The incidence of ocular events in the eye under investtigation was similar between patients receiving 6mg faricimab (pooled n=284 [42.8%]) and aflibercept 2mg (pooled n=285 [43.1%]). The Review Group note that the SmPC for faricimab was updated following the detection of new post authorisation safety signals for retinal vasculitis and retinal occlusive vasculitis. In the RHONE-X extension study no cases of retinal vasculitis and retinal occlusive vasculitis were detected and rates of ocular inflammation were 1.8%. Reported safety data from the Applicant's NMA suggest that there were no marked differences in the safety profile or rates of discontinuation across all anti-VEGF IVTs.

3. Cost effectiveness of faricimab

Methods

The Applicant compared the cost of faricimab to existing anti-VEGF treatments (aflibercept, ranibizumab and bevacizumab). The Applicant assumed equal efficacy, utility and safety of faricimab (T&E) to existing anti-VEGF treatments (PRN) in their heath-economic model based on the NMA. Therefore, only number of injections, administration visits and monitoring visits were modelled separately across treatments. The Review Group note the limitations of the NMA and the associated uncertainties in the assumption of equal efficacy. Data for faricimab (T&E) was derived from the YOSEMITE and RHINE trials' data up to Year 2 whereas data for the comparators came from the NMA in Year 1 and the Protocol T study (which compared aflibercept, ranibizumab and bevacizumab administered by PRN protocol) thereafter. The Review Group note that none of the comparator trials derived from the NMA permitted once

q.16.w injection administration frequency intervals. A maximum treatment duration of 5 years was assumed for the majority (85%) of patients alive and on treatment in the health-economic model.

Results

An incremental analysis of the lifetime costs of faricimab (T&E) versus aflibercept (PRN), ranibizumab (PRN) and bevacizumab (PRN) was presented by the Applicant (Table 1). The Applicant base case estimated the incremental lifetime costs of faricimab to be lower (i.e. cost saving) when compared to aflibercept (PRN), but higher (i.e. more costly) than ranibizumab (PRN) and bevacizumab (PRN).

Table 1: Applicant base case incremental cost results a,b,c

Lifetime Costs	Faricimab 6mg (€)	Ranibizumab 0.5mg (PRN) (€)	Aflibercept 2mg (PRN) (€)	Bevacizumab 1.25mg (PRN) (€)
Drug acquisition cost	24,619	19,425	24,179	6.952
Administration cost	9,968	11,138	11,170	12,038
Monitoring costs	2,533	5,136	5,275	4,879
Mean total cost	37,120	35,699	40,624	23,869
Incremental cost (faricimab versus comparator)	N/A	+1,421	- 3,504	+ 13,251

N/A: Not applicable

[a] Cost of visual impairment was removed from Applicant's base case.

b Corresponding probabilistic incremental cost using 1,000 iterations = +€1,914 (vs ranibizumab), -€3,202 (vs aflibercept) and +€14,242 (vs bevacizumab). Figures in the table are rounded, and so calculations may not be directly replicable

C *Total costs and QALYs presented are discounted (4%).*

The Review Group identified several limitations in the Applicant's base case. Those limitations that were addressed in the NCPE adjusted base case included an updated rebate rate and drug acquisition cost for bevacizumab (Table 2).

Table 2: NCPE adjusted base case incremental cost results [a,b,c]

Lifetime Costs	Faricimab 6mg (€)	Ranibizumab 0.5mg (PRN) (€)	Aflibercept 2mg (PRN) (€)	Bevacizumab 1.25mg (PRN) (€)
Drug acquisition cost	24,619	19,425	24,179	5,917
Administration cost	9,968	11,138	11,170	12,038
Monitoring costs	2,533	5,136	5,275	4,879
Mean total cost	37,120	35,699	40,624	22,834
Incremental cost (faricimab versus comparator)	N/a	+1,421	-3,504	+14,286

[a] *Corresponding probabilistic incremental cost using 1,000 iterations = +€1,940 (vs ranibizumab), -€2,835 (vs aflibercept) and +€15,235 (vs bevacizumab). Figures in the table are rounded, and so calculations may not be directly replicable cTotal costs and QALYs presented are*

discounted (4%).

Sensitivity analysis

A key scenario conducted by the Review Group included the assumption of biosimilar product availability for ranibizumab and aflibercept towards the end of 2025. Using biosimilar prices for both (assumed to be a 45% rebate on the price to wholesaler [PtW]) the incremental lifetime costs for faricimab (T&E) increased considerably versus ranibizumab (+ €10,573) and aflibercept (+ €7,888) administered by PRN protocol.

4. Budget impact of faricimab

The price to wholesaler of faricimab is €853 per pack (1 vial). The estimated cost of faricimab per-patient, per-treatment course is informed by the mean number of injections administered in YOSEMITE and RHINE in Year 1 and 2, and the NMA for all anti-VEGF comparators (bevacizumab, aflibercept and ranibizumab PRN) and from the mean number of injections administered in the Protocol T study for subsequent years (from Year 3 onwards).

The Applicant estimated that 7,511 patients would receive treatment with faricimab over five years. The NCPE adjusted five-year cumulative gross drug budget impact for faricimab is €35.63 million (including VAT), and the five-year net drug budget impact is €3.93 million (including VAT). There is considerable uncertainty associated with the budget impact estimates which do not allow for any displacement of bevacizumab in the model. The Review Group conducted several scenarios including: 1) assuming the introduction of biosimilar products (ranibizumab, aflibercept), the resultant five-year net drug budget impact would be about €18.7 million; 2) increasing the market share or faricimab up to 100% at year five given the purported lower number of injections required, the resultant five-year net drug budget impact would be about €54.12 million; 3) assuming biosimilar prices for aflibercept and ranibizumab and that faricimab displaces all existing anti-VEGF interventions , the resultant five-year net drug budget impact would be about €72.35 million.

5. Patient Organisation Submission

A patient organisation submission was received from Fighting Blindness.

6. Conclusion

The NCPE recommends that faricimab not be considered for reimbursement unless cost effectiveness can be improved relative to existing treatments*.

*This recommendation should be considered while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013.