NCPE Assessment

Technical Summary

Faricimab (Vabysmo®)

22060

30 June 2025

Applicant: Roche Products Ireland Ltd

Faricimab for the treatment of adults with neovascular age-related macular degeneration.

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] treatments in adults with neovascular age-related macular degeneration (nAMD). There are an estimated 134,174 patients with age-related macular degeneration (AMD) in Ireland, of which nAMD is estimated to occur in approximately 10%. This equates to approximately 16,194 patients with nAMD. Reimbursement of faricimab in public hospitals is sought.

Faricimab is a humanised bispecific immunoglobulin G1 antibody that acts through inhibition of two distinct pathways by neutralisation of both angiopoietin-2 and vascular endothelial growth factor A. 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 maintenance doses can be individualised to either every eight weeks (q.8.w), every twelve weeks (q.12.w) or every sixteen weeks (q.16.w). Faricimab is intended for long-term use as per the Summary of Product Characteristics (SmPC).

Four anti-VEGF therapies are authorised by the European Commission for the treatment of nAMD; aflibercept (Eylea®), brolucizumab (Beovu®) ranibizumab (Lucentis®) and most recently bevacizumab (Lytenava®). No anti-VEGF treatment is centrally reimbursed within Ireland or has undergone a NCPE Health Technology Assessment. Clinical opinion obtained by the Review Group indicated an unlicensed preparation of bevacizumab is predominantly prescribed as a first-line therapy in patients with nAMD in Ireland. Clinical opinion also indicated that aflibercept and ranibizumab are prescribed as alternative first- or second-line therapies in Ireland (dependent on what treatment(s) are available in each hospital). Brolucizumab is not used in the Irish treatment setting and has not been included as a comparator, which the Review Group consider appropriate. Clinical opinion reported that a treat and extend (T&E) protocol is routinely used in clinical practice in Ireland. The Applicant anticipates that faricimab will be used as a second-line treatment after first-line anti-VEGF treatment. However, the licensed indication for faricimab does make any restrictions based on line of therapy in patients with nAMD. The clinical trial evidence supporting product registration was conducted in treatment-naïve patients with nAMD. The Review Group do

not consider the Applicant's assumption that faricimab will be used as a second-line treatment appropriate. It is possible that faricimab could also be used in the first-line setting, as per the licence, if reimbursed, unless gatekeeping measures are implemented by the HSE.

1. Comparative effectiveness of faricimab

The efficacy and safety of faricimab was assessed in two phase III, randomised, double-blind, active comparator non-inferiority trials (TENAYA and LUCERNE, n=671) in anti-VEGF naïve participants. Faricimab 6mg was administered via a single IVT injection q.4.w up to week 12, followed by maintenance doses q.8.w, q.12.w or q.16.w, (based on disease activity assessment) up to week 60. From week 60, patients were administered faricimab according to a personalised treatment interval (PTI)), in which adjustment of intervals was based on disease activity up to week 108. Aflibercept 2mg was administered via a single IVT injection q.4.w up to week 8, followed by a fixed injection frequency (q.8.w up to week 108). The primary endpoint was change from baseline in best corrected visual acuity (BCVA). Both trials met their primary efficacy endpoint, demonstrating that faricimab was non-inferior to aflibercept. The Review Group consider the following key limitations; both trials included treatment-naïve patients, however, the Applicant anticipates that faricimab will only be used in the second-line setting if reimbursed; the PTI approach was not permitted in the comparator arm and permitted in the faricimab arm (with a PTI of up to q.16.w).

The comparative effectiveness analysis utilised a network meta-analysis (NMA) in a Bayesian framework to inform the comparison between faricimab and comparators aflibercept, ranibizumab and bevacizumab administered according to all administration protocols; T&E, pro re nata (PRN) and fixed dose administration. For the purposes of constructing evidence networks, different doses and treatment administration schedules of the same drug were considered to be distinct interventions. All outcomes were assessed at one year, with mean number of injections and BCVA also assessed at two years. A total of 44 studies were included in the NMA. All studies enrolled participants with nAMD. The majority of studies enrolled anti-VEGF naïve participants exclusively, in line with TENAYA and LUCERNE, though four studies enrolled pre-treated participants. There were notable differences in baseline patient characteristics between the studies, including differences in mean baseline BCVA and in distributions of age, sex and ethnicity. There is likely to be substantial between-study heterogeneity in the trials deemed eligible for inclusion in the NMA. This may result in bias in the resulting treatment effect estimates. There were also differences between trials in the

number of loading doses administered, and in protocols used to define the T&E approach. Of note, unlike the majority of other trials in the network (excluding the ARIES trial), the TENAYA and LUCERNE trials allowed for longer dosing intervals of q.16.w and intervals which could be maintained or extended in the presence of worsening BCVA (provided central subfield thickness did not increase by more than 10% compared with the reference value). This may have led to fewer faricimab injections being administered, compared with other anti-VEGF treatments in the evidence network with more stringent requirements for extending dosing intervals.

Results of the Applicant's NMA suggest that vision outcomes and safety were similar across all anti-VEGF therapies and dosing regimens. Applying the non-inferiority criteria from TENAYA and LUCERNE to the NMA results, faricimab given via a T&E approach may be regarded as non-inferior versus all comparators in the network for the primary outcome of BCVA at 12 months, and furthermore, equivalent to aflibercept (T&E) and ranibizumab (T&E), as well as having high probability of equivalence to bevacizumab (T&E). Analysis of other vision outcomes supported this conclusion. The mean number of injections at 12 and 24 months were numerically lower for faricimab (T&E) compared with other anti-VEGF treatments (T&E), however, these differences were not statistically significant. The Review Group therefore consider it possible that the numerical reduction in mean injection numbers may be partly or fully explained by chance effects and the differences in T&E protocols between studies. Therefore, the Review Group consider that Applicant's key claim, namely that faricimab will lead to a reduced injection frequency compared to other anti-VEGF therapies administered according to T&E approaches, has not been established.

2. Safety of faricimab

The SmPC for faricimab reports the most frequently reported adverse events (AEs) were cataract (10%), conjunctival haemorrhage (7%), vitreous detachment (4%), intraocular pressure increased (4%), vitreous floaters (4%), eye pain (3%), and retinal pigment epithelial tear (3%). The most serious AEs were uveitis (0.5%), endophthalmitis (0.4%), vitritis (0.4%), retinal tear (0.2%), hematogenous retinal detachment (0.1%), and traumatic cataract (<0.1%). The SmPC carries special warnings for: retinal vasculitis and retinal occlusive vasculitis; product-class-related adverse reactions; immunogenicity; IVT injection-related reactions and intraocular pressure increases.

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 (T&E) in their heath-economic model based on the findings of the NMA, that faricimab exhibits similar in efficacy in terms of BCVA and safety when compared to comparator anti-VEGF therapies; administered by T&E protocol. The Review Group re-iterate the limitations of the NMA and the associated uncertainties in the assumption of equal efficacy.

A Markov model was used to capture all costs and outcomes. The model comprised visual acuity (VA)-related health states and transitions for both eyes, as well as treatment-related health states and transitions for both eyes. Patients (in which one eye is assumed to have nAMD) enter the model as treatment commences. Transition probabilities for disease efficacy differ by visual acuity (VA). Treatment switching was not implicitly allowed in the model and the Review Group highlight that treatment switching between anti-VEGF therapies can occur in clinical practice in Ireland. Thus, if the model considers first-line treatment, switching treatment should be included. The Applicant however anticipates that faricimab, if reimbursed, will be used only in the second-line setting. In this setting, the Review Group consider it reasonable not to model subsequent treatments. However, the evidence for faricimab is from treatment-naïve patients. A lifetime horizon (25 years) was used. Model cycles were four weeks.

Results

An incremental analysis of the costs of faricimab versus aflibercept, ranibizumab and bevacizumab was presented by the Applicant (Table 1).

Table 1: Applicant base case incremental cost results[a]

Lifetime Cost	Faricimab 6mg (T&E) (€)	Ranibizumab 0.5mg (T&E) (€)	Aflibercept 2mg (T&E) (€)	Bevacizumab 1.25mg (T&E) (€)
Intervention cost	34,036	34,944	34,444	13,814
IVT injection administration cost	12,606	18,355	14,551	21,930
Cost of visual impairment	25,953	25,953	25,953	25,953
Mean total cost	72,596	79,253	74,949	61,698
Incremental cost vs faricimab	N/A	-6,657	-2,353	+10,898

***IVT**: intravitreal; N/A: not applicable*

[a] Corresponding probabilistic incremental cost using 1,000 iterations = -€7,731 (vs ranibizumab), -€3,983 (vs aflibercept 2mg) and €9,126 (vs bevacizumab). Figures in the table are rounded, and so calculations may not be directly replicable Total costs and QALYs presented are discounted (4%).

The Review Group identified a number of limitations in the Applicant's base case which were addressed in the NCPE adjusted base case (Table 2). The lower annual number of injections for faricimab compared to comparator treatments in year three and beyond is not supported by evidence. In the NCPE adjusted base case, the annual number of injections was assumed to be equal across all anti-VEGF treatments in year three and beyond.

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

Lifetime Cost	Faricimab 6mg (T&E) (€)	Ranibizumab 0.5mg (T&E) (€)	Aflibercept 2mg (T&E) (€)	Bevacizumab 1.25mg (T&E) (€)
Intervention cost	34,023	27,720	31,693	8,746
IVT injection administration cost	12,601	14,467	13,359	15,539
Cost of visual impairment	25,953	25,953	25,953	25,953
Mean total cost	72,577	68,140	71,005	50,238
Incremental cost vs faricimab	N/A	+4,437	+1,572	+22,339

***IVT**: intravitreal; **N/A**: not applicable*

[a] Corresponding probabilistic incremental cost using 1,000 iterations=€4,479 (vs ranibizumab), €1,612 (vs aflibercept) and €22,194 (vs bevacizumab). Figures in the table are rounded, and so calculations may not be directly replicable. Total 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]) and the hospital contract price, obtained by the Review Group, for bevacizumab, the incremental costs for faricimab versus ranibizumab (+€15,403), faricimab versus aflibercept (+€14,110) and faricimab versus bevacizumab (+€30,448) increased considerably.

4. Budget impact of faricimab

The PtW of faricimab is €853 per pack (one vial). The estimated cost of faricimab per-patient, per-treatment course is €6,593.01 (including VAT) in Year One and €4,239.75 per annum in Year Two onwards, based on the mean number injections per year derived from the TENAYA and LUCERNE trials for faricimab and the NMA for all anti-VEGF comparators (T&E). The Applicant estimated that 13,427 patients would receive treatment with faricimab over five years. The NCPE adjusted five-year cumulative gross drug budget impact for faricimab is €69.15 million (including VAT), and the five-year net drug budget impact is €7.38 million (including VAT). There is considerable uncertainty associated with the budget impact

estimates. The Review Group conducted several scenarios including: 1) assuming the introduction of biosimilar products (ranibizumab, aflibercept) and a hospital contract price for bevacizumab [five-year net drug budget impact €21.32 million]; 2) increasing the market share or faricimab up to 100% at Year Five given the purported advantages associated with the treatment including a longer injection interval and the lower number of injections [five-year net drug budget impact €83.62 million]; 3) increasing the market share for faricimab up to 100% at Year Five and incorporating biosimilar costs and hospital contract prices [five-year net drug budget impact €123.60 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.