Surrey Heartlands Integrated Care System
Area Prescribing Committee (APC)

Integrated Care Partnership - Surrey Downs, Guildford & Waverley, North-West Surrey, and East Surrey Places & associated partner organisations

Evidence review

Medicine details	
Name, brand name	Aflibercept 8mg in 0.07ml injection Eylea® 114.3 mg/ml solution for injection[1]
Manufacturer	Bayer
Licensed Indication	Eylea is indicated in adults for the treatment of - neovascular (wet) age-related macular degeneration (nAMD)[1] - visual impairment due to diabetic macular oedema (DMO)[1]
Proposed indication	To be prescribed where dose extension beyond 8 weeks is not possible with the lower dose injection, aflibercept 2mg.
Requested by	Surrey Heartlands Medicines Ophthalmology Network

Evidence Review

Relevant guidance / reviews

NICE (National Institute for Health and Care Excellence) decided not to evaluate aflibercept 8 mg for a Health Technology Evaluation because they determined it to be clinically equivalent and at least as cost-effective as the already recommended aflibercept 2 mg formulation[2]. Given this equivalence, NICE concluded that conducting a separate evaluation for the 8 mg dose would not be an efficient use of NHS resources

The NHSE Medicines Value & Access team[3] is undertaking work on current and future treatment pathways in medical retinal services, specifically looking at wet age-related macular degeneration, diabetic macular oedema and retinal vein occlusion.

They have reminded Trusts and ICBs that the aflibercept 2mg treat and extend protocol offers the opportunity to extend treatment duration up to 16 weeks. This should be tried first prior to moving patients to newer treatments.

The anticipated savings associated with the launch of aflibercept biosimilar 2mg. Current spend for the branded product is over £300m nationally per annum so biosimilars present a significant cost saving opportunity

The Medicines Value & Access team is using a data-driven approach to understand outcomes, activity, and cost assumptions for different treatments. Despite challenges in accessing real-world NHS data, they are developing a model to support local decision-making. In collaboration with specialists and the national clinical director, they have created start, switch, and stop criteria to ensure patients receive the best value treatment. These criteria support shared decision-making between patients and clinicians to start the most appropriate treatment and stop it if it is ineffective, not beneficial, or causing harm.

It is expected that their new commissioning recommendations will be available between April 2025 and the launch of the aflibercept 2mg biosimilar injection, this application is intended to make aflibercept 8mg available for patients who are not responding satisfactorily to the 2mg dose, but without impeding maximum implementation of the biosimilar aflibercept (2mg) when it becomes available later this year.

Current intelligence suggests that biosimilar versions of 8mg aflibercept are unlikely to enter the market in 2025/26.

Clinical Effectiveness

Aflibercept 8 mg has demonstrated significant efficacy in clinical trials for treating retinal conditions such as neovascular (wet) age-related macular degeneration (nAMD) and diabetic macular oedema (DMO). The PULSAR and PHOTON trials showed that aflibercept 8 mg, with extended dosing intervals of 12 or 16 weeks, achieved non-inferior visual acuity gains compared to the standard 2 mg dose administered every 8 weeks.

As can be seen in the NICE communication, the proposal is that this extended dosing interval can substantially reduce the treatment burden for patients, potentially improving adherence and outcomes[4]

It is important to note, however, that aflibercept 2mg injection is licensed for Treat and Extend protocol with intervals up to 16 weeks, and this was not reflected in the trials where the aflibercept 2mg dose was given regularly every 8 weeks. It is also important to note that some patients in the 8mg injection trial required injections more frequently than 12 weekly, and therefore patients still need to be evaluated at 8 weeks.

The volume injected with the aflibercept 8mg dose is 40% greater than that with the aflibercept 2mg dose. Some clinicians have expressed concern, however clinical trials have shown that the safety profile of aflibercept 8 mg is consistent with that of the 2 mg dose.

More real-world data is needed to fully understand the long-term safety and efficacy of the higher dose, as clinical trials did not compare like-for-like treat and extend regimens, and may not capture all potential issues

More information will become available when the Medicines Value & Access team issue their recommendations, and the Area Prescribing Committee may be asked to review current pathways accordingly if different.

Safety

The safety profile of aflibercept 8 mg is consistent with that of the 2 mg dose. No new safety signals were identified in the clinical trials[3,4]. Common adverse events included ocular discomfort, increased intraocular pressure, and cataracts, which are typical for intravitreal injections[3,4..]

Patient factors

The proposed place in therapy (in patients on Treat and Extend Protocols who cannot extend dose intervals beyond 8-weekly injections) will enable patients with an insufficient response to the 2mg dose, to intensify treatment to the 8mg dose, thus potentially increasing intervals between treatments which would be very welcome
The proposed place in therapy does not include treatment naïve patients - it is possible that the higher 8mg dose will allow faster escalation of doses than the 2mg dose, however the trials did not maximise the potential to increase dose intervals between the 2mg doses to its' maximum 16 week intervals, and therefore more evidence is required, especially as there is the potential for significant cost savings with the imminent availability of biosimilar aflibercept.
There is more long term experience with the aflibercept 2mg dose which enhances evidence of safety.

Impact to Secondary/ specialist care

As the population ages, the prevalence of age-related retinal diseases, such as age-related macular degeneration (AMD), increases. Older adults are more susceptible to these conditions due to the natural aging process of the eye.

Advances in medical care have improved the management of chronic conditions like diabetes and hypertension. While this has increased life expectancy, it has also led to a higher incidence of diabetic retinopathy and other retinal diseases associated with these conditions.

Enhanced diagnostic technologies, such as optical coherence tomography (OCT), have improved the detection and monitoring of retinal diseases, leading to more diagnoses.

These factors combined contribute to the rising number of retinal disease cases.

As a result, this has significantly impacted the capacity of ophthalmology clinics in the UK, without the accompanying resources of workforce. Any opportunity to reduce the number of appointments and injections will be welcome.

Not all units have the organization to deliver treat and extend protocols, and for those units, it is unlikely to be useful to introduce newer medicines where the Treat and Extend benefits cannot be materialized.

Impact to Primary Care

There is no expected impact to Primary Care

Cost implications

It is expected that, when biosimilar aflibercept 2mg becomes available later in 2025, that this will release significant savings to the NHS.
The manufacturers of the aflibercept 8mg injection (the same as that for the originator aflibercept 2mg injection) have provided significant savings compared to the current price for the originator 2mg dose, and compared to the other second/ third line treatments, faricimab and brolucizumab.

Summarize decisions in other areas

South West London[6] – aflibercept approved, dose not specified

Special Considerations

As recommended by the Medicines Value & Access team, the proposed place in therapy is as follows:
Aflibercept 2mg injection should either be prescribed after biosimilar ranibizumab or 1st line for the treatment of wet AMD and Diabetic Macular Oedema, with a Treat and Extend protocol aiming to increase injection intervals up to 16 weeks where possible.
The local additional recommendations are:
Where the dose intervals for aflibercept cannot be extended beyond 8mg intervals (or dose intervals after that) then the aflibercept 8mg dose may be prescribed. It is proposed that if the increase dose does not allow for the increased dosage intervals after 3-6 months, the prescription should be converted back to aflibercept (biosimilar when it becomes available)
Aflibercept 8mg is less expensive than faricimab and brolucizumab and should therefore be used ahead of these alternatives unless a patient has experienced an adverse reaction specific to aflibercept or an allergic reaction.

Recommendation to APC

It is proposed that Aflibercept 8mg injection is added as an option for patients with wetAMD or DMO who do not respond sufficiently to the aflibercept 2mg dose in Treat and Extend Protocols.
Extension to 16week intervals should be attempted before changing from the 2mg dose to the 8mg dose, and, if benefit is not seen after 3-6 months, the 2mg aflibercept dose (biosimilar when it becomes available) should be re-instated/
Aflibercept 8mg injection is less expensive than faricimab and therefore should be used in preference when the aflibercept 2mg dose is insufficient.

Other considerations

Updated pathways for wetAMD and DMO will be taking these decisions into account.

The pathways will need to be reviewed once the National Commissioning recommendations are published.

References

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3. E-mail communication from NHSE Medicines Value & Access team
4. Brown DM, Boyer DS, Do DV, Wykoff CC, Sakamoto T, Win P, et al. Intravitreal aflibercept 8 mg in diabetic macular oedema (PHOTON): 48-week results from a randomised, double-masked, non-inferiority, phase 2/3 trial. Lancet (London, England) [Internet]. 2024 Mar 23 [cited 2024 Jun 4];403(10432):1153–63. Available from: https://pubmed.ncbi.nlm.nih.gov/38461843/
5. Wykoff CC, Brown DM, Reed K, Berliner AJ, Gerstenblith AT, Breazna A, et al. Effect of High-Dose Intravitreal Aflibercept, 8 mg, in Patients With Neovascular Age-Related Macular Degeneration. JAMA Ophthalmology. 2023 Sep 1;141(9):834–4.
6. South West London Formulary, accessed February 2025, https://www.swljointmedicinesformulary.nhs.uk/chaptersSubDetails.asp?FormularySectionID=11&SubSectionRef=11.08.02&SubSectionID=D100&drugmatch=4545#4545

Equality Impact Assessment

Protected characteristics Protected Characteristics - Information	**Describe any considerations or concerns for each group.**	**Describe suggested mitigations to reduce inequalities.**
Age	Older people will find it harder to attend hospital for injections. So reduced injection frequency would be welcome Trials do not reflect the very old and frail patients who receive these treatments.	There needs to be continued monitoring of real world data to establish which of the newer treatments have real benefits over the established treatments. Unfortunately the trials did not provide a fair comparison and more research is required There is more experience in this group of patients with the long-established treatments: ranibizumab and aflibercept.
Disability	As this treatment is designed to treat and avoid deterioration of eyesight, many of the patients	This is covered by fair access to treatment

	will have a degree of visual impairment	
Gender reassignment	N/A	
Marriage and civil partnership	N/A	
Pregnancy & maternity	N/A	
Race	N/A	
Religion and belief	N/A	
Sex	N/A	
Sexual orientation	N/A	
Impact on any other vulnerable groups?	N/A	

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Declaration of Interest:

None

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Reviewed by:

Appendix 1

To find medicine safety alerts in the UK and abroad, including those from the FDA, you can use the following resources:

1. **UK - Medicines and Healthcare products Regulatory Agency (MHRA)**:
    - The MHRA publishes alerts, recalls, and safety information for drugs and medical devices. You can access these updates on their official website.
2. **USA - Food and Drug Administration (FDA)**:
    - The FDA provides safety alerts and recalls for medications and medical devices. You can find this information on the FDA's MedWatch website.
3. **European Medicines Agency (EMA)**:
    - The EMA offers safety updates and alerts for medicines authorized in the European Union. Visit the EMA's website for more details.
4. **Central Alerting System (CAS)**:
    - In the UK, the CAS provides access to urgent safety guidance and alerts. You can search for new and past alerts on the CAS website

These resources will help you stay informed about the latest safety alerts and recalls for medicines both in the UK and internationally.