Health Technology Briefing
March 2026

EYE103 for treating diabetic macular oedema

Company/Developer	Merck Sharp & Dohme Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 37555	NICE ID: Not Available	UKPS ID: 675273

Licensing and Market Availability Plans

Currently in phase II/III clinical development.

Summary

EYE103 is in clinical development for the treatment of diabetic macular oedema (DMO). DMO is the most common cause of vision loss in people with diabetes. It affects the macula, which is the central part of the retina and is needed for clear, detailed vision. DMO develops when high blood sugar damages the small blood vessels in the eye, causing them to leak fluid into the macula. This fluid build-up makes the macula swell, which can lead to blurred or distorted vision. The risk of developing DMO is greater for people who have had diabetes for a long time, have poorly controlled blood sugar, high blood pressure or high cholesterol levels, who smoke or are pregnant.

EYE103 is an antibody (a type of protein) designed to strengthen the eye's natural barrier that normally stops fluid from leaking into the macula. By reducing this leakage, EYE103 may help lessen swelling in the retina and protect vision. Many people with DMO do not fully respond to current treatments, and fluid can remain in the retina despite regular injections. EYE103 is a new type of medicine that is delivered by intravitreal injection (an injection into the eye). It works in a different way from existing treatments, which may help improve vision for patients whose disease is not well controlled with current therapies. If licensed, EYE103 would offer an additional treatment option for patients with DMO.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.
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Proposed Indication

Treatment of patients with diabetic macular oedema (DMO).[1]

Technology

Description

EYE103 (Restoret) is a tetravalent, tri-specific Wingless-related integration site (Wnt) agonist antibody delivered by intravitreal injection. Restoret mimics the natural ligand Norrin, which agonises the Wnt signalling pathway. Norrin is crucial in restoring and maintaining the blood-retinal barrier by inducing tight junction organisation, limiting vascular permeability.[2]

EYE103 is currently in clinical development for the treatment of DMO. In the phase II/III clinical trial BRUNELLO (NCT06571045), patients are given a high dose or low dose of EYE103 by intravitreal injection.[1]

Key Innovation

More than 30% of patients experience suboptimal response or persistent oedema on current anti-vascular endothelial growth factor (VEGF) therapies, suggesting other pathogenic factors, beyond VEGF, might contribute to the pathogenesis of DMO.[3] EYE103 is a potentially first-in-class treatment for DMO.[4] EYE103 agonises the Wnt signalling pathway, which is implicated in restoring and maintaining the integrity of the blood-retinal barrier to reduce vascular leakage.[4] By targeting the Wnt pathway, EYE103 seeks to resolve residual retinal fluid and improve visual outcomes in patients who continue to exhibit persistent oedema despite anti-VEGF treatment.[3,5]

If licensed, EYE103 would provide an additional treatment option for patients with DMO.

Regulatory & Development Status

EYE103 does not currently have marketing authorisation in the EU/UK for any indication.

EYE103 is not in phase II/III clinical development for any other indication.

Patient Group

Disease Area and Clinical Need

DMO is the most common cause of sight loss in people with diabetes. It affects the central area of the retina, called the macula, which is responsible for fine detail vision both near and far away. DMO occurs when blood vessels damaged by high blood sugar leak into the macular region, resulting in a fluid build-up.[6,7] This build-up of fluid causes swelling of the macula which can impair sight. People with both type 1 and type 2 diabetes are at risk of DMO. The risk of developing DMO is greater for people who have had diabetes for a long time, have poorly controlled blood sugar, high blood pressure or high cholesterol levels, who smoke or are pregnant.[8] In the early stages of diabetes, a person may not notice any effect on their vision as damage to the retina occurs over many years. However, when the blood vessels in or close to the macula become damaged, or there is sudden bleeding or fluid leaking into the macula, then sight can worsen dramatically.[6]

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According to the UK's national ophthalmology database study in 2013, clinically significant macular oedema was present in 6,664 eyes, 13.9% of the total number of diabetic eyes with structured assessment data at the time of their last record.[9] The prevalence of DMO in the UK diabetic population is approximately 7%, and around 39% of these patients will have clinically significant DMO - reducing the visual acuity to poorer than 6/6 in at least one eye. Approximately 2.7% of UK diabetes patients experience clinically significant DMO with visual impairment.[10] In England (2024/25), there were 1,143 hospital admissions for patients with type 1 diabetes with ophthalmic complications (ICD-10 code E10.3, which includes DMO), and 1,614 finished consultant episodes (FCEs), resulting in 2,742 FCE bed days and 685 day cases. There were 2,390 hospital admissions for patients with type 2 diabetes with ophthalmic complications (ICD-10 code E11.3, which includes DMO), and 2,995 FCEs, resulting in 3,981 FCE bed days and 1,645 day cases.[11]

Recommended Treatment Options

DMO is usually treated with either laser treatment or intravitreal injections.[12] The National Institute for Health and Care Excellence (NICE) recommends pharmacological therapies for DMO in eyes with central retinal thickness >400µm. NICE does not recommend licensed pharmacological therapies for DMO in eyes with CRT <400 µm.[13] These can either be anti-VEGF injections or steroids.

NICE currently recommends the following therapies for the treatment of DMO:

- Ranibizumab[14]
- Aflibercept[15]
- Dexamethasone[16]
- Brolucizumab[17]
- Faricimab[18]

Clinical Trial Information

Trial	**BAROLO, NCT06957080;** A Randomized, Double-Masked, Multi-Center, 3-Arm Pivotal Phase 2/3 Study to Evaluate The Efficacy and Safety of Intravitreal EYE103 Compared With Intravitreal Ranibizumab (0.5mg) in Participants With Diabetic Macular Edema **Phase II/III –** Active, not recruiting **Location(s):** USA and other countries **Primary completion date:** March 2027
Trial Design	Randomised, parallel assignment, quadruple masked
Population	N=1054 (actual); subjects with type 1 or 2 diabetes mellitus and DMO; age 18 years and older.
Intervention(s)	Intravitreal administration of EYE103
Comparator(s)	Intravitreal administration of ranibizumab
Outcome(s)	Primary outcome: change from baseline best-corrected visual acuity measured using the standardised ETDRS chart [time frame: 52 weeks] See trial record for full list of other outcomes.
Results (efficacy)	-

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Results (safety)	-

Trial	**BRUNELLO,** NCT06571045; A Randomized, Double-Masked, Multi-Center, 3-Arm Pivotal Phase 2/3 Study to Evaluate The Efficacy and Safety of Intravitreal EYE103 Compared With Intravitreal Ranibizumab (0.5mg) in Participants With Diabetic Macular Edema **Phase II/III –** Active, not recruiting **Location(s):** 12 EU countries, UK, US and other countries **Primary completion date:** September 2026
Trial Design	Randomised, parallel assignment, quadruple masked
Population	N=984 (actual); subjects with type 1 or 2 diabetes mellitus and DMO; age 18 years and older.
Intervention(s)	Intravitreal administration of EYE103
Comparator(s)	Intravitreal administration of ranibizumab
Outcome(s)	Primary outcome: change from baseline best-corrected visual acuity measured using the standardized ETDRS chart [time frame: 52 weeks] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Trial	**AMARONE,** NCT05919693; A 2-part Study Consisting of an Open-label Multiple Ascending Dose (MAD) Safety Study, and a Dose-finding Single-masked Comparative Safety and Preliminary Efficacy Study of Intravitreal (IVT) EYE103 in a Mixed Population of Participants With Diabetic Macular Edema (DME) or Neovascular Age-related Macular Degeneration (NVAMD) **Phase I/II –** Completed **Location(s):** UK, USA, Argentina and Puerto Rico **Primary completion date**: August 2024
Trial Design	Part 1: Sequential assignment Part 2: Randomised, single masked
Population	N=33 (actual); subjects with DMO or NVAMD; DMO patients must be ≥ 18 years of age, NVAMD patients must be ≥ 50 years of age.
Intervention(s)	Intravitreal administration of EYE103
Comparator(s)	No comparator
Outcome(s)	Primary outcome: adverse events [time frame: 3 months]. See trial record for full list of other outcomes.

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Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of EYE103 is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Ranibizumab port delivery system for treating diabetic macular oedema (GID-TA11065). Expected date of issue to be confirmed.
- NICE technology appraisal. Ranibizumab for treating diabetic macular oedema (TA274). October 2023.
- NICE technology appraisal. Dexamethasone Intravitreal implant for treating diabetic macular oedema (TA824). September 2022.
- NICE technology appraisal. Brolucizumab for treating diabetic macular oedema (TA820). August 2022.
- NICE technology appraisal. Faricimab for treating diabetic macular oedema (TA799). June 2022.
- NICE technology appraisal. Aflibercept for treating diabetic macular oedema (TA346). July 2015.
- NICE clinical guideline. Type 2 diabetes in adults: management (NG28). February 2026
- NICE clinical guideline. Type 1 diabetes in adults: diagnosis and management (NG17). August 2022.

NHS England (Policy/Commissioning) Guidance

No relevant guidance identified.

Other Guidance

- Amoaku WM, Ghanchi F, Bailey C, *et al.* Diabetic retinopathy and diabetic macular oedema pathways and management: UK Consensus Working Group. 2020.[13]
- Scottish Intercollegiate Guidelines Network. Management of diabetes: a national clinical guideline. 2017.[19]
- European Society of Retina Specialists (EURETINA). Guidelines for the management of diabetic macular edema by EURETINA. 2017.[20]

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NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.

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