New Medicine Assessment

Fenofibrate to Reduce Progression of Diabetic Retinopathy

Recommendation: Amber 0 for the following indications:

Reduce the progression of diabetic retinopathy for people with non-proliferative retinopathy and type 2 diabetes.

Summary of supporting evidence:

- Fenofibrate is an established medicine for cardiovascular disease with well document safety and monitoring information but is unlicensed for use in diabetic retinopathy.
- NICE states that ophthalmologists should consider fenofibrate for people with non-proliferative retinopathy and type 2 diabetes to reduce the progression of diabetic retinopathy.
- The original data came from cardiovascular outcome trials but was substantiated by the LENS trial 2023.
- Evidence to date shows a reduction in the progression to and progression of diabetic retinopathy, but not other outcomes such as visual acuity or quality of life.
- Patients may experience transient increases in serum transaminases. Monitoring required.
- Contraindicated if estimated glomerular filtration rate < 30 mL/min/1.73 m^2. Renal monitoring required.
- Interactions with oral vitamin K antagonists, ciclosporin and statins.
- Low annual costs per patient.
- Cost-effectiveness modelling suggested that fenofibrate results in a mean reduction in health service costs.
- Expected downstream cost savings from fewer patients developing progressive diabetic retinopathy and requiring laser or intravitreal injections.
- Existing Green RAG in cardiovascular disease.
- Cheshire and Mersey list fenofibrate as Amber Recommended for diabetic retinopathy.

Details of Review

Name of medicine (generic & brand name)**:**

Fenofibrate

Strength(s) and form(s):

Micronised 160mg tablets

Micronised 67mg capsules

Micronised 200mg capsules

Micronised 267mg capsules

Dose and administration:[1]

By mouth using capsules

Initially 200 mg daily, then increased if necessary to 267 mg daily, maximum 200 mg daily with

concomitant statin, 267 mg capsules not appropriate for initial dose titration.

By mouth using tablets

160 mg daily.

BNF therapeutic class / mode of action:

Fibrate - Fibrates act by decreasing serum triglycerides; they have variable effect on LDL-cholesterol.

Licensed indication(s):[2]

Adjunct to diet and other non-pharmacological treatment (e.g. exercise, weight reduction) for the following:

- Treatment of severe hypertriglyceridaemia with or without low HDL cholesterol.

- Mixed hyperlipidaemia when a statin is contraindicated or not tolerated.

- Mixed hyperlipidaemia in patients at high cardiovascular risk in addition to a statin when triglycerides and HDL cholesterol are not adequately controlled.

Proposed use (if different from, or in addition to, licensed indication above):

To reduce the progression of diabetic retinopathy (unlicensed indication).

Course and cost:

Fenofibrate micronised 160mg tablets x 28 £2.38

Fenofibrate micronised 200mg capsules x 28 £3.15

Fenofibrate micronised 267mg capsules x 28 £5.61

Fenofibrate micronised 67mg capsules x 90 £13.74

Proposed dose 200mg once daily = **£37.80/patient/year**

Drug tariff price January 2026

Current standard of care/comparator therapies:

- Lowering HbA1c
- Lowering BP
- Fenofibrate (unlicensed)
- Laser treatment
- Panretinal photocoagulation
- Anti-vascular endothelial growth factor medicines (anti-VEGFs)

Relevant NICE guidance:

NG242: Diabetic retinopathy: management and monitoring | Guidance | NICE

Background and context

Diabetic retinopathy (DR) remains a major cause of sight loss worldwide, despite new therapies and improvements in the metabolic control of people living with diabetes. Therefore, DR creates a physical and psychological burden for people, and an economic burden for society. Fenofibrate may be a useful strategy to achieve this goal, by reversing diabetes' effects and reducing inflammation in the retina, as well as improving dyslipidaemia and hypertriglyceridaemia.[4]

An application was received from Lancashire Teaching Hospitals Trust for the use of fenofibrate in diabetic

retinopathy. The application requested RAG Amber 0.

Current formulary entry

02.12 Lipid-regulating drugs

Fenofibrate BNF SPC BNF C	**Formulary** GREEN	Capsules (micronised) 200mg, 267mg Tablets (micronised) 160mg

MHRA: Fibrates: first-line treatment not recommended

Summary of evidence

Summary of efficacy data in proposed use:

NICE[3] (2024)

Ophthalmologists should consider fenofibrate for people with non-proliferative retinopathy and type 2 diabetes to reduce the progression of diabetic retinopathy.

Evidence from 2 randomised controlled trials showed fenofibrate is beneficial for people with type 2 diabetes and retinopathy at baseline. However, evidence was only available for retinopathy progression. There was no evidence on other outcomes such as visual acuity or quality of life. Despite this, the committee thought the evidence showed an important effect. They were aware that this is currently (August 2024) an off-label use of fenofibrate. They therefore thought that it should be ophthalmologists who consider prescribing fenofibrate and who initiate their prescription where appropriate. GPs can then renew the prescription.

There was no evidence on the effects of other types of fibrates, or on fenofibrate for people with type 1 diabetes, so they were not included in the recommendation. However, the committee was aware of ongoing research on the effects of fibrates for this group, so they decided against making a recommendation for research. The committee highlighted that there is limited evidence on how effective fibrates are at preventing diabetic retinopathy progression in people from a range of ethnic backgrounds. They felt this was an important consideration and therefore made a recommendation for research on fibrates to prevent progression of diabetic retinopathy. The recommendation is likely to increase the use of fenofibrate in people with non-proliferative diabetic retinopathy, but this can reduce the risk of progression, thereby reducing the time and costs associated with additional treatment.

Cochrane[4] (2023)

We included two studies and their eye sub-studies (15,313 participants) in people with T2D. The studies were conducted in the US, Canada, Australia, Finland, and New Zealand; follow-up period was four to five years. One was funded by the government, the other by industry.

Compared to placebo or observation, fenofibrate likely results in little to no difference in progression of DR (risk ratio (RR) 0.86; 95% confidence interval (CI) 0.60 to 1.25; 1 study, 1012 participants; moderate-certainty evidence) in a population with and without overt retinopathy at baseline. Those without overt retinopathy at baseline showed little or no progression (RR 1.00, 95% CI 0.68 to 1.47; 1 study, 804 participants); those with overt retinopathy at baseline found that their DR progressed slowly (RR 0.21, 95% CI 0.06 to 0.71; 1 study, 208 people; test for interaction P = 0.02).

Compared to placebo or observation, fenofibrate likely resulted in little to no difference in either the incidence of overt retinopathy (RR 0.91; 95% CI 0.76 to 1.09; 2 studies, 1631 participants; moderate-certainty evidence); or the incidence of diabetic macular oedema (RR 0.39; 95% CI 0.12 to 1.24; 1 study, 1012 participants; moderate-certainty evidence).

The use of fenofibrate increased severe adverse effects (RR 1.55; 95% CI 1.05 to 2.27; 2 studies, 15,313 participants; high-certainty evidence).

The studies did not report on incidence of a reduction in visual acuity of 10 ETDRS letters or more, incidence of proliferative diabetic retinopathy, or mean vision-related quality of life.

Current, moderate-certainty evidence suggests that in a mixed group of people with and without overt retinopathy, who live with T2D, fenofibrate likely results in little to no difference in progression of diabetic

retinopathy. However, in people with overt retinopathy who live with T2D, fenofibrate likely reduces the progression.

Comparison of the main fenofibrate studies[5] (2025)

- **FIELD** (Fenofibrate Intervention and Event Lowering in Diabetes) was a multicenter, randomised clinical trial in which almost 10,000 adults with type 2 diabetes (T2DM) not taking any lipid-modifying therapy were randomly assigned to receive fenofibrate 200 mg or placebo for the prevention of major adverse cardiovascular endpoints over 5 years. Even though fenofibrate did not reduce the risk of developing the primary outcome, the cumulative incidence of requirement for photocoagulation was 5.2% in the placebo group, versus 3.6% in the fenofibrate group. This prompted a more detailed sub-analysis of ocular endpoints, which showed a significant reduction of the requirement for laser treatment for macular oedema (HR 0.69, 95% CI 0.54–0.87) and of proliferative DR (HR 0.70, 95% CI 0.52–0.87) in the fenofibrate group relative to placebo.
- **ACCORD** (Action to Control Cardiovascular Risk in Diabetes) was a randomised trial in which more than 10,000 adult patients with T2DM were randomized in a three-way factorial design to a tight versus usual glycemic control strategy, tight versus usual blood pressure control strategy and fenofibrate versus placebo over a 3.5-year follow-up. The sub-analysis that focused on ophthalmologic endpoints included 1,593 participants with fundoscopic examination. The rate of progression of diabetic retinopathy at 4 years was 6.5% with fenofibrate versus 10.2% with placebo (aOR 0.60, 95% CI 0.42–0.87).
- **LENS** (Lowering Events in Non-Proliferative Retinopathy) trial. Participants were patients with diabetes (26% type 1) and non-referable diabetic retinopathy, who were randomised to receive fenofibrate 145 mg or placebo. The main outcome was a composite of progression to diabetic retinopathy, referable maculopathy or treatment for either one. Making use of the fundoscopic images, the study also examined separately the incidence of other ocular outcomes. The HR for the primary outcome comparing the fenofibrate group versus placebo was 0.73 (95% CI 0.58–0.91). Other secondary outcomes were also significantly reduced, including any progression of diabetic retinopathy (HR 0.74, 95% CI 0.61–0.90), exudates or retinal haemorrhages (HR 0.66, 95% CI 0.52–0.85) and macular oedema (HR 0.50, 95% CI 0.30–0.84).

  Similar to other fenofibrate studies, there was a 7.9 ml/min reduction in the trial-averaged estimated glomerular filtration rate (eGFR) in the fenofibrate group. This effect is believed to be caused by either a fenofibrate-induced reduction in tubular creatinine secretion, or increased tissular production of creatinine, none of which represents a true deterioration of glomerular function.

Table 1 Main characteristics of clinical trials with fenofibrate that analyzed ocular endpoints

	FIELD sub-study	ACCORD-EYE	LENS
Study type	RCT	RCT	RCT
Years of execution	1998–2005	2001–2009	2018–2023
Location	Australia, New Zealand, and Finland	United States	Scotland
Inclusion criteria	Age 50–75 T2DM TC/HDLc > = 4 TG 1–5 mmol/l	Age 40–79 with CVD, or age 55–79 without CVD T2DM HbA1c 7–11% High CVD risk	Age > = 18 Diabetes (not gestational) Non-referable DR
Sample size	9795 (1012 in eye sub-study)	2856 (1593 in fenofibrate sub-study)	1151
Active arm intervention	Fenofibrate 200 mg/day	Fenofibrate 160 mg/day in the background of Simvastatin 20–40 mg	Fenofibrate 145 mg/day
Comparator	Placebo	Placebo	Placebo
Primary endpoint	> = 2-step increase in ETDRS	> = 3-step increase in ETDRS or requirement for photocoagulation or vitrectomy	New referable DR/maculopathy, or treatment for DR or maculopathy
Main results	HR for any retinopathy 0.69 (0.56–0.84) Requirement for photocoagulation 5.2% with placebo vs. 3.6 with fenofibrate	Progression of DR 6.5% with fenofibrate vs. 10.2% with placebo, OR 0.60 (0.42–0.87)	HR for primary endpoint 0.73 (0.58–0.91) HR for new exudates or retinal hemorrhages 0.66 (0.52–0.85) HR for macular edema 0.50 (0.30–0.84)

RCT randomized controlled trial, *T2DM* type 2 diabetes, *CVD* cardiovascular disease, *TC* total cholesterol, *HDLc* HDL cholesterol, *TG* triglycerides, *DR* diabetic retinopathy, *ETDRS* Early Treatment Diabetic Retinopathy Study Scale, *HR* hazard ratio, *OR* odds ratio

Summary of safety data:

Summary of Product Characteristics[2]

Contraindications

- Hypersensitivity to the active substance or to any of the excipients
- Hepatic insufficiency (including biliary cirrhosis and unexplained persistent liver function abnormality)
- Known gallbladder disease
- Severe renal insufficiency (estimated glomerular filtration rate < 30 mL/min/1.73 m^2)
- Chronic or acute pancreatitis with the exception of acute pancreatitis due to severe hypertriglyceridemia
- Known photoallergy or phototoxic reaction during treatment with fibrates or ketoprofen

Precautions for use

- **Liver function -** As with other lipid lowering agents, increases have been reported in transaminase

levels in some patients. In the majority of cases these elevations were transient, minor and asymptomatic.

- **Pancreas -** Pancreatitis has been reported. In the FIELD-study, a statistically significant increase in pancreatitis cases was observed in patients receiving fenofibrate versus patients receiving placebo (0.8% versus 0.5%; p = 0.031).
- **Muscle -** Muscle toxicity, including rare cases of rhabdomyolysis, with or without renal failure has been reported with administration of fibrates and other lipid-lowering agents. The incidence of this disorder increases in cases of hypoalbuminaemia and previous renal insufficiency. Patients with pre-disposing factors for myopathy and/or rhabdomyolysis, including age above 70 years, personal or familial history of hereditary muscular disorders, renal impairment, hypothyroidism and high alcohol intake, may be at an increased risk of developing rhabdomyolysis.

  Muscle toxicity should be suspected in patients presenting diffuse myalgia, myositis, muscular cramps and weakness and/or marked increases in CPK (levels exceeding 5 times the normal range). In such cases treatment with fenofibrate should be stopped.
- **Renal function -** Fenofibrate 200 mg is contraindicated in severe renal impairment. Fenofibrate 200 mg should be used with caution in patients with mild to moderate renal insufficiency. Dose should be adjusted in patients whose estimated glomerular filtration rate is 30 to 59 mL/min/1.73 m^2.

  Reversible elevations in serum creatinine have been reported in patients receiving fenofibrate monotherapy or co-administered with statins. Elevations in serum creatinine were generally stable over time with no evidence for continued increases in serum creatinine with long term therapy and tended to return to baseline following discontinuation of treatment.

  During clinical trials, 10% of patients had a creatinine increase from baseline greater than 30 µmol/L with co-administered fenofibrate and simvastatin versus 4.4% with statin monotherapy. 0.3% of patients receiving co-administration had clinically relevant increases in creatinine to values > 200 µmol/L. Treatment should be interrupted when creatinine level is 50% above the upper limit of normal. It is recommended that creatinine is measured during the first three months after initiation of treatment and thereafter periodically.

Interactions

- **Oral vitamin K antagonists -** Fenofibrate enhances oral anti-coagulant effect and may increase risk of bleeding.
- **Ciclosporin -** Some severe cases of reversible renal function impairment have been reported.
- **HMG-CoA reductase inhibitors or other fibrates -** The risk of serious muscle toxicity is increased if a fibrate is used concomitantly with HMG-CoA reductase inhibitors or other fibrates.
- **Glitazones -** Some cases of reversible paradoxical reduction of HDL-cholesterol have been reported.

Undesirable effects

The most commonly reported ADRs during Fenofibrate therapy are digestive, gastric or intestinal disorders.

For a comprehensive list of the undesirable effects of fenofibrate please see product SPC.

Strengths and limitations of the evidence:

Strengths

- Fenofibrate is an established medicine for cardiovascular disease with well document safety and monitoring information
- The recently published LENS trial substantiates indirect evidence of benefit from previous cardiovascular outcome trials
- Cost-effectiveness modelling suggested that fenofibrate results in a mean reduction in health service costs

Limitations

- Comparators to placebo, but unlikely to see trials comparing to anti-VEGF injections
- Evidence shows a reduction in the progression to and progression of diabetic retinopathy, but not other

outcomes such as visual acuity or quality of life

Summary of evidence on cost effectiveness:

Cost-effectiveness of fenofibrate versus standard care[6]

Resource use and outcome data were collected over follow-up for participants enrolled in LENS. Mean costs were compared at 2 years and per 6- month follow-up (median 4.0 years). Within the trial, cost-effectiveness was assessed in terms of the incremental cost per case of referable disease averted. A microsimulation model, with inputs derived primarily from LENS trial data, was used to assess the incremental cost per quality-adjusted life year (QALY).

Fenofibrate resulted in a mean (95% confidence interval) reduction in health service costs of -£254 (−1062 to 624) at 2 years and -£101 (−243 to 42) per 6-month follow-up. This was accompanied by a 4.4% (1.3% to 8.0%) absolute reduction in any referable diabetic retinopathy or treatment thereof at 2 years, and a 27% (9%–42%) relative reduction over follow-up. Modelled over 10 years, fenofibrate use cost an additional £6 per patient for an expected QALY gain of 0.02, costing £406 per QALY versus standard care under base case assumptions. The probability of cost-effectiveness varied from 70% to 79% at a threshold of £20,000 per QALY, depending on the price discount applied to anti-VEGF drugs. Fenofibrate is likely to offer a cost-effective treatment for slowing the progression of diabetic retinopathy in people with early to moderate diabetic retinopathy or maculopathy.

Prescribing and risk management issues:

Monitoring[2]

Renal

Fenofibrate should not be used if severe renal impairment, defined as eGFR <30 mL/min per 1.73 m2, is present. If eGFR is between 30 and 59 mL/min per 1.73 m2, the dose of fenofibrate should not exceed 100 mg standard or 67 mg micronized once daily. If, during follow-up, the eGFR decreases persistently to <30 mL/min per 1.73 m2, fenofibrate should be discontinued.

Special care needed in patients with renal disease, as progressive increases in serum creatinine concentration or failure to follow dosage guidelines may result in myotoxicity (rhabdomyolysis). Monitor serum creatinine levels during the first 3 months of treatment and periodically thereafter—interrupt treatment if creatinine level is 50% above the upper limit of normal.

Hepatic

It is recommended that transaminase levels are monitored every 3 months during the first 12 months of treatment and thereafter periodically. Attention should be paid to patients who develop increase in transaminase levels and therapy should be discontinued if AST (SGOT) and ALT (SGPT) levels increase to more than 3 times the upper limit of the normal range. When symptoms indicative of hepatitis occur (e.g. jaundice, pruritus), and diagnosis is confirmed by laboratory testing, fenofibrate therapy should be discontinued.

Commissioning considerations:

Innovation, need and equity implications of the intervention:
Potential for the reduction of progressive diabetic retinopathy and therefore reduction in the need for invasive intravitreal injections.
Financial implications of the intervention:
Proposed dose 200mg once daily = **£37.80/patient/year** Lancashire Teaching Hospitals anticipate 450 patients per year at their Trust. Extrapolate to 3 Trusts = 450 x 3 = 1,350 patients

1,350 x £37.80 = **£51,030 estimated ICB drug cost/year**

Expected downstream cost savings from fewer patients developing progressive DR and requiring laser or intravitreal injections (cost range: £80–£700 per procedure). Cost savings likely from reduced use of consumables, equipment for intravitreal injections and staff time.

E.g. Ranibizumab >£500 per injection.

Service Impact Issues Identified:

None identified.

Equality and Inclusion Issues Identified:

None identified.

Cross Border Issues Identified:

Cheshire and Mersey list fenofibrate as **AR** (Amber Recommended requires specialist assessment and recommendation to GP to prescribe in Primary Care) to reduce progression of diabetic retinopathy in Type 2 Diabetes.

They also have a document to support the recommendation.

GMMMG list fenofibrate as **SA** (Green following specialist advice). This is listed in the cardiovascular chapter with no indications.

Legal Issues Identified:

None identified.

Media/ Public Interest:

None identified.

Grading of evidence (based on SORT criteria):

Levels	Criteria	Notes
Level 1	Patient-oriented evidence from: • high quality randomised controlled trials (RCTs) with low risk of bias • systematic reviews or meta-analyses of RCTs with consistent findings	High quality individual RCT= allocation concealed, blinding if possible, intention-to-treat analysis, adequate statistical power, adequate follow-up (greater than 80%)
Level 2	Patient-oriented evidence from: • clinical trials at moderate or high risk of bias • systematic reviews or meta-analyses of such clinical trials or with inconsistent findings • cohort studies • case-control studies	
Level 3	Disease-oriented evidence, or evidence from: • consensus guidelines • expert opinion • case series	Any trial with disease-oriented evidence is Level 3, irrespective of quality

References

[1] British National Formulary, 'Fenofibrate', 2025 [Accessed Jan 2026]

[2] Summary of Product Characteristics, 'Fenofibrate 200 mg Capsules', 2023 [Accessed Jan 2026]

[3] National Institute for Health and Care Excellence, 'NG242: Diabetic retinopathy: management and monitoring', 2024 [Accessed Jan 2026]

[4] Kataoka SY et al, 'Fenofibrate for diabetic retinopathy', *Cochrane Database of Systematic Reviews,* 2023 [Accessed Jan 2026]

[5] Parra-Pineda A et al, 'Fenofibrate and Diabetic Retinopathy', *Diabetes Therapy*, vol. 16, 1763–1777 (2025).

[6] Scotland G et al, 'Cost-effectiveness of fenofibrate versus standard care for reducing the progression of diabetic retinopathy: An economic evaluation based on data from the LENS trial', *Diabetic Medicine,* vol. 42, 2025