

Latanoprost–netarsudil for previously treated primary open-angle glaucoma or ocular hypertension

Technology appraisal guidance

Published: 2 October 2024

www.nice.org.uk/guidance/ta1009

Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the [Yellow Card Scheme](#).

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should [assess and reduce the environmental impact of implementing NICE recommendations](#) wherever possible.

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1 Recommendations

- 1.1 Latanoprost–netarsudil is recommended as an option for reducing intraocular pressure (IOP) in adults with primary open-angle glaucoma or ocular hypertension when a prostaglandin analogue alone has not reduced IOP enough, only if:
- they have then tried a fixed-dose combination treatment and it has not reduced IOP enough, or
 - a fixed-dose combination treatment containing beta-blockers is unsuitable.
- 1.2 This recommendation is not intended to affect treatment with latanoprost–netarsudil that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop.

Why the committee made these recommendations

Usual treatment for reducing IOP in people with primary open-angle glaucoma or ocular hypertension includes a prostaglandin analogue eye drop (for example, bimatoprost or latanoprost). If this does not work well enough, people usually have a fixed-dose combination treatment eye drop. These include combinations of a prostaglandin analogue with a beta-blocker (for example, bimatoprost–timolol), or a prostaglandin analogue with carbonic anhydrase inhibitors or sympathomimetics.

Latanoprost–netarsudil is a fixed-dose combination treatment containing a prostaglandin analogue with a Rho kinase inhibitor. For this evaluation, the company asked for latanoprost–netarsudil to be considered only after a fixed-dose combination treatment has not worked well enough or when a fixed-dose combination treatment with a beta-blocker is unsuitable.

Clinical trial evidence suggests that latanoprost–netarsudil is as effective as bimatoprost–timolol. Indirect comparisons of latanoprost–netarsudil with other fixed-dose combination treatments are highly uncertain, but suggest that they have similar

effectiveness.

A cost comparison suggests that latanoprost–netarsudil has similar or lower costs than most branded fixed-dose combination treatments. These are usually used after a fixed-dose combination treatment has not reduced IOP enough. Latanoprost–netarsudil also has similar or lower costs compared with some generic fixed-dose combination treatments. So, latanoprost–netarsudil is recommended.

2 Information about latanoprost–netarsudil

Marketing authorisation indication

- 2.1 Latanoprost–netarsudil (Roclanda, Santen) is indicated 'for the reduction of elevated intraocular pressure (IOP) in adult patients with primary open-angle glaucoma or ocular hypertension for whom monotherapy with a prostaglandin or netarsudil provides insufficient IOP reduction'.

Dosage in the marketing authorisation

- 2.2 The dosage schedule is available in the [summary of product characteristics for latanoprost–netarsudil](#).

Price

- 2.3 The list price for latanoprost–netarsudil is £10.00 per 2.5-ml bottle (excluding VAT; company submission, April 2024, subject to approval).
- 2.4 Costs may vary in different settings because of negotiated procurement discounts.

3 Committee discussion

The [evaluation committee](#) considered evidence submitted by Santen, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the [committee papers](#) for full details of the evidence.

The condition

Effects on quality of life

- 3.1 Glaucoma and ocular hypertension (OHT) are associated with increased pressure within the eye, known as intraocular pressure (IOP). Increased IOP is caused by production of too much aqueous humour in the eye or decreased drainage of this fluid (or a combination of these factors). A build-up of too much pressure in the eye causes damage to the optic nerve, ultimately leading to progressive and irreversible visual impairment. Primary open-angle glaucoma (POAG) is the most common form of glaucoma in the UK. People with progressive visual impairment experience a substantial impact on quality of life, often needing assistance from family or other carers for daily activities. Increased IOP may not impact quality of life if it has not progressed to glaucoma with damage to the optic nerve. But the patient experts explained that both OHT and glaucoma can have a negative impact on quality of life because of the burden of treatments to reduce IOP. It is not uncommon for people with OHT or glaucoma to be using multiple eye drops, some of which must be used multiple times per day. One patient expert explained that self-administering multiple eye drops is more manageable at home. When away from home, it can become more challenging because of the need to always carry multiple medications around. Some people are dependent on others to help them with administering the drops, but this is not always possible. The clinical experts explained that in clinical practice, some eye drops are preferred over others owing to differences in side effect profiles and clinician experience. Some bottles may also be harder to use than others, which can impact on quality of life. A clinical expert further explained that eye redness is not uncommon with latanoprost–netarsudil, but it is not usually uncomfortable and is reversible. While it can be intolerable for some people, others are very willing to have eye redness if it prevents vision loss or avoids surgery. The patient experts explained that

OHT and glaucoma also have a considerable psychological impact because of the uncertainty of the prognosis. Because increased IOP is asymptomatic, people are often unaware of how the condition is progressing and it is very difficult to predict when vision loss will occur and to what extent. IOP is currently the only modifiable risk factor for glaucoma. The patient experts explained that people sometimes feel powerless because there are no lifestyle or other factors that they can change to improve their prognosis. The committee concluded that people with OHT or POAG would benefit from further once-daily treatment options that prevent vision loss.

Clinical management

Treatment options

- 3.2 People with OHT or POAG are usually first offered treatment with selective laser trabeculoplasty (SLT). If this surgery is unsuitable or is declined, a generic prostaglandin analogue monotherapy eye drop will be offered (for example, bimatoprost, latanoprost, tafluprost or travoprost). If SLT or generic prostaglandin analogue monotherapy, or both, have failed to adequately lower IOP, then a medicine from another therapeutic class can be added. These include beta-blockers (for example, betaxolol, carteolol hydrochloride, levobunolol hydrochloride or timolol maleate), carbonic anhydrase inhibitors (for example, acetazolamide, brinzolamide or dorzolamide) or sympathomimetics (for example, apraclonidine or brimonidine tartrate). These treatments can be used as monotherapy eye drops, but the clinical experts explained that fixed-dose combination treatments are often preferred. This is because of the complementary modes of action between different therapeutic classes, and because it limits the number of drops people need to take each day. Commonly used fixed-dose combinations include bimatoprost–timolol, brimonidine–timolol, brinzolamide–brimonidine, brinzolamide–timolol, dorzolamide–timolol, latanoprost–timolol, tafluprost–timolol, or travoprost–timolol. If IOP remains uncontrolled after treatment with medicines from 2 therapeutic classes, a further SLT procedure or another surgical procedure such as trabeculectomy may be offered. These procedures are in addition to continued treatment with eye drop medicines. The patient experts explained that while most people with POAG wish

to avoid surgery for as long as possible, repeated surgeries when medicines fail to adequately lower IOP are not uncommon. The committee noted that, unlike most of the fixed-dose combination treatments, latanoprost–netarsudil does not contain a beta-blocker. It concluded that latanoprost–netarsudil would be a useful treatment option, particularly for people for whom beta-blockers are contraindicated or not suitable.

Comparators

- 3.3 The clinical experts explained that the most relevant point in the treatment pathway for fixed-dose combination treatments is after initial SLT or prostaglandin analogue monotherapy eye drops, or both. The choice of fixed-dose combination treatment depends on several factors, including the healthcare professional and person's preferences, and whether the person can tolerate a specific class of treatment, such as beta-blockers. It is not uncommon that some older people cannot tolerate beta-blockers, particularly if they have a respiratory condition such as asthma or chronic obstructive pulmonary disorder. The clinical experts emphasised that controlling IOP is often a case of trial and error, and of trying different combinations of eye drops to avoid surgery for as long as possible. For this reason, the clinical experts explained that no single fixed-dose combination treatment is an obvious comparator for latanoprost–netarsudil. The committee concluded that all fixed-dose combination eye drops should be considered as relevant comparators for latanoprost–netarsudil.

Clinical effectiveness

MERCURY 3 trial

- 3.4 The clinical data for latanoprost–netarsudil came from MERCURY 3, a phase 3, double-blind, randomised controlled trial comparing latanoprost–netarsudil with bimatoprost–timolol. It included adults with POAG or OHT in both eyes who had previous monotherapy and were considered by the investigators to need combination treatment. Their medicated IOP was 17 mmHg or more in at least 1 eye and below 28 mmHg in both eyes at the initial screening visit. The primary

endpoint in MERCURY 3 was mean IOP within each treatment group at the following time points: 8am, 10am and 4pm at the week 2, week 6 and month 3 study visits. The results of the trial are confidential and cannot be reported here. Clinical non-inferiority of latanoprost–netarsudil relative to bimatoprost–timolol was shown with the upper limit of the 95% confidence intervals being:

- 1.5 mmHg or lower at all time points
- 1.0 mmHg or lower at 6 out of 9 time points from week 2 through to month 3.

The committee agreed that the trial population adequately reflected the licensed population for latanoprost–netarsudil. It concluded that the results of the trial showed the clinical non-inferiority of latanoprost–netarsudil compared with bimatoprost–timolol.

Indirect treatment comparisons

3.5 Because MERCURY 3 only compared against bimatoprost–timolol, the company did a network meta-analysis to compare latanoprost–netarsudil with other relevant fixed-dose combination treatments. Because of limitations in the evidence base, the company decided to use monotherapy trials to create a bridge between 2 unconnected parts of the network. The EAG explained that the company's approach was reasonable, but that there was a lack of transparency in how it selected the specific monotherapy trials to include. The EAG therefore was concerned about the possibility that the selection of trials could have biased the network meta-analysis results in favour of latanoprost–netarsudil. The company explained that its literature search and process for excluding trials from the analysis was systematic, and that any potential bias would be random and not in favour of latanoprost–netarsudil. The company explained that it had provided its base-case analysis (using a random effects model) and a sensitivity analysis (using a fixed effects model). The resulting treatment effect from these 2 network meta-analyses was comparable, with both indicating no difference in effect between different treatments. The committee considered whether the company's base-case analysis was sufficiently systematic. It agreed that any revised network meta-analyses would inevitably involve trade-offs between potential sources of uncertainty, such as trial heterogeneity, so would be unlikely to provide more robust results. It concluded that the company's network meta-

analyses suggested that differences in treatment effect between latanoprost–netarsudil and the relevant comparators was small.

Economic model

Cost–utility model time horizon

3.6 The company's original evidence submission presented a cost–utility model comparing latanoprost–netarsudil with all other fixed-dose combination eye drops. The Markov model used 4 health states, 3 representing IOP reduction from baseline (less than 20%, 20% to 30%, and more than 30%), and the absorbing death state. The model had a lifetime time horizon of 33 years, from a starting age of 67 up to age 100. The company stated that it chose a lifetime horizon to enable monitoring of disease progression over a person's lifetime. But the EAG disagreed that the model structure was capturing disease progression. It noted that the model did not capture the costs and quality-adjusted life-year benefits of slowing conversion from OHT to glaucoma, or glaucoma disease progression. This is because while IOP is an important modifiable risk factor for glaucoma, it is only a surrogate marker for symptomatic disease. The EAG further noted that alternative health states could have been explored, such as mild, moderate and severe disease. This would have more closely matched disease progression as experienced by people with the condition. The model also allowed transitions between any of the 3 non-death health states, but this implicitly assumed that vision loss caused by glaucoma is reversible, which is not clinically plausible.

In response to these concerns, the company submitted a revised model at the technical engagement stage. This model had a reduced time horizon of 12 months. The company stated that the reduced time horizon avoided the need to make unrealistic assumptions and extrapolations when there was limited data to establish a link between short- and long-term disease progression. It noted that it also removed uncertainty around the impacts of treatment discontinuation. But the EAG maintained its view that more appropriate models could have been explored that would have been better suited to capture conversion from OHT to glaucoma and progression of glaucoma over time. It agreed with the company that using a 12-month time horizon reduced some of the uncertainty caused by

extrapolating clinical effectiveness in the model. It also noted that assuming no significant differences in clinical efficacy between the intervention and comparators (see [section 3.5](#)) made it possible to focus on differences in costs over the shorter-term treatment period, because these drove cost effectiveness. The EAG commented that if this model and approach were accepted by the committee, it would be similar to a cost-effectiveness evaluation using a cost-comparison approach. The committee concluded that the company's original lifetime time horizon was appropriate, but that the model was unsuitable for capturing disease progression. The committee noted that because of the assumed similar efficacy of latanoprost–netarsudil and the comparators, and the uncertainties in the network meta-analyses, there would be little benefit in requesting an alternative cost–utility model over a lifetime time horizon. It agreed with the company and EAG that a 12-month time horizon would be appropriate for a cost-comparison approach. But it further concluded that the company's cost–utility model was not suitable for a cost-comparison evaluation, and requested that the company submit a full cost-comparison model.

Cost-comparison model

3.7 The company submitted a new cost-comparison model that maintained the time horizon at 12 months and allowed treatment discontinuation to be excluded (see [section 3.6](#)). The company reiterated that the 12-month time horizon was chosen to reflect a person's short-term treatment rather than a full lifetime on treatment. The EAG stated again that it should have been possible to develop an economic model that captured conversion from OHT to glaucoma and progression of glaucoma over time. For example, using Markov states defined by OHT and glaucoma stage. But it also agreed that the company's approach of a 12-month time horizon and focus on costs removed concerns about capturing disease progression in the economic model. The committee considered the company's new cost-comparison model and concluded that it was appropriate for decision making.

Company's optimised position for latanoprost–netarsudil

3.8 On submission of its cost-comparison model, the company explained that clinical

experts expected that latanoprost–netarsudil, along with most branded fixed-dose combination comparator treatments, would usually be considered after a generic fixed-dose combination treatment had not reduced IOP enough. It would also be considered after monotherapy with a prostaglandin analogue if a fixed-dose combination treatment containing beta-blockers was unsuitable. The committee concluded that the company's optimised position for latanoprost–netarsudil in the treatment pathway was appropriate.

Costs

Adverse event resource use

- 3.9 The company's original economic model included adverse events of any severity, occurring in at least 5% of people in either the latanoprost–netarsudil or bimatoprost–timolol arm of MERCURY 3. The EAG explained that the company had not modelled adverse events by severity. So, its economic model assumed a more intensive use of secondary care resources to manage mild and moderate adverse events than would be expected in UK clinical practice. In response to these concerns, the company adjusted its resource use to reflect severity as reported in MERCURY 3. Mild adverse events were assumed to not need any resource use and were excluded. For moderate adverse events, the company assumed that resource use was in line with the EAG's preferred lower cost assumptions. For severe adverse events, resource use remained in line with the company's original model, in which assumptions on resource costs had been validated by clinical expert opinion. The EAG noted that the incremental adverse event costs were broadly similar between the company's revised approach and its preferred approach to costing resource use for severe adverse events. It also noted that it had little impact on the overall cost-effectiveness results. The committee noted that the company's revised approach to adverse event resource costs was used in its cost-comparison model. It concluded that it would consider both approaches in its decision making.

Acquisition costs

3.10 The clinical experts explained that latanoprost–netarsudil and the comparators are most likely to be started in secondary care, then prescribed routinely in primary care. The company and EAG agreed that primary care prescribing costs should be considered for the evaluation. The company used market share estimates based on 2022 sales data, with trends from 2015 to 2022 extrapolated at the same trajectory for 2023 to 2028. It preferred NHS indicative prices for branded products, obtained from the BNF, but the drug tariff prices for the share of the market prescribed as generics. The EAG agreed that the market share data provided by the company accurately reflected current prescribing, and that a mix of branded and generic products will likely be prescribed in UK clinical practice. But the EAG explained its preference for drug tariff prices for all treatments, because these prices more accurately capture the price paid to pharmacies for dispensing treatments in primary care. The committee considered the impact on the incremental cost of both the EAG's and company's preferred cost assumptions. It concluded that it would consider both in its decision making.

Cost-effectiveness estimates

Company's cost-comparison results

3.11 The company did a cost-minimisation analysis comparing latanoprost–netarsudil with 23 branded and generic fixed-dose combination products in a population of people with POAG or OHT. The committee recalled that latanoprost–netarsudil is anticipated to be positioned in the same line of treatment as other branded products after insufficient reduction in IOP with a prostaglandin analogue and a generic fixed-dose combination eye drop (see [section 3.8](#)). In the company's base-case analysis, latanoprost–netarsudil was associated with lower total costs per person than 13 of 23 branded and generic comparators. This showed that latanoprost–netarsudil is likely to have similar or lower costs than a large proportion of the current market. When compared with branded products only, latanoprost–netarsudil was associated with lower total costs per person than 11 of 18 branded products. The committee concluded that, on average, latanoprost–netarsudil is likely to have similar or lower costs compared with other

fixed-dose combination treatments that would be used in clinical practice. So latanoprost–netarsudil is recommended.

Other factors

Equality

3.12 Stakeholders noted that the risk of glaucoma differs between ethnic groups. The committee was not provided with any evidence for latanoprost–netarsudil for separate ethnic groups. It concluded that no adjustments to the recommendation were needed. Stakeholders also noted that once-daily treatments may reduce inequalities by providing a simpler treatment regimen for people or their carers who may have challenges with using multiple eye drops. They also noted that some additives such as preservatives can cause intolerance in people with cornea damage. The committee further concluded that patients and clinicians should take these issues into account when considering latanoprost–netarsudil, but that no adjustments to the recommendation were needed.

Innovation

3.13 The committee considered if latanoprost–netarsudil was innovative. It did not identify additional benefits of latanoprost–netarsudil not captured in the economic modelling. So, the committee concluded that latanoprost–netarsudil was not innovative for treating POAG or OHT.

Conclusion

Recommendation

3.14 The committee concluded that latanoprost–netarsudil was cost effective when used after monotherapy with a prostaglandin analogue, and when a fixed-dose combination treatment provides insufficient reduction of IOP, or a fixed-dose

combination treatment containing beta-blockers is contraindicated or unsuitable. So, latanoprost–netarsudil is recommended.

4 Implementation

- 4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 3 months of its date of publication.
- 4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final draft guidance.
- 4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has ocular hypertension or primary open-angle glaucoma and the healthcare professional responsible for their care thinks that latanoprost–netarsudil is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by [committee D](#).

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The [minutes of each evaluation committee meeting](#), which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Megan John

Chair, technology appraisal committee D evaluation committee

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser and a project manager.

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ISBN: 978-1-4731-6127-6