NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Netarsudil for treating open angle glaucoma or ocular hypertension

Draft scope to project manager for consultation

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of netarsudil within its marketing authorisation for treating open angle glaucoma or ocular hypertension.

Background

Glaucoma refers to a group of eye conditions characterised by progressive damage to the optic nerve. It can lead to impaired peripheral vision and eventually total loss of sight, if it is not detected and treated early. Glaucoma is usually associated with an increase in pressure within the eye. This can be caused by either the production of too much aqueous humour by the ciliary body or decreased outflow (drainage) of the fluid.

Ocular hypertension (OHT) is the term used to describe elevated intraocular pressure (IOP; that is IOP greater than 21 mmHg) in the absence of optic nerve damage or visual field loss. It can be present for many years without the development of glaucoma, however sustained elevation of IOP causes damage to the optic nerve head and is a major risk factor for the development of glaucoma. Lowering OHT has been shown to lower the risk of developing glaucoma.

Primary, or chronic, open-angle glaucoma (COAG) accounts for over 70% of all glaucoma cases[1]. It develops slowly over many years and doesn't cause any noticeable symptoms until irreversible damage has occurred to the optic nerve. The peripheral vision is affected first, and without treatment, central vision may also be lost resulting in loss of visual acuity.

Open-angle glaucoma had an estimated UK prevalence in 2017 of approximately 2% of people over the age of 40 years[2,3]. Using the 2019 ONS population projections[4] this would be more than approximately 660,000 in the UK. The overall risk of developing glaucoma increases substantially with increasing IOP and with age. OHT is estimated to affect 3-5% of people over the age of 40 years (2015 prevalence)[5], which could be over 1 million people in England[4]. However, the number of people requiring treatment is expected to be much lower than this.

NICE's guidance on the diagnosis and management of glaucoma (NG81) recommends a generic prostaglandin analogue for people with IOP of 24 mmHg or more if they are at risk of visual impairment within their lifetime. For those who cannot tolerate their current treatment, an alternative generic prostaglandin analogue should be offered, and if this is not tolerated, a beta-blocker. If none of these options are tolerated (or not reducing IOP sufficiently), non-generic prostaglandin analogues, carbonic anhydrase inhibitors, sympathomimetics, miotics or a combination of treatments should be offered. People whose IOP cannot be reduced sufficiently with pharmacological treatment should be referred to a consultant ophthalmologist to discuss other options.

A generic prostaglandin analogue is offered to people with confirmed COAG. For people with advanced COAG, surgery with pharmacological augmentation is offered (with interim treatment with a generic prostaglandin analogue while listed for surgery). If adherence and eye drop instillation technique are satisfactory but IOP has not been reduced sufficiently to prevent the risk of progression to sight loss despite pharmacological treatment, or the drug is not tolerated, a drug from another therapeutic class can be offered (beta-blocker, carbonic anhydrase inhibitor or sympathomimetic), and topical drugs from different therapeutic classes may be needed at the same time to control IOP. Alternatively, laser trabeculoplasty or surgery with pharmacological augmentation can be offered.

The technology

Netarsudil (Rhokiinsa, Aerie Pharmaceuticals) inhibits both Rho kinase and the norepinephrine transporter which increases fluid outflow and reduces fluid inflow. It is administered as an eye drop.

Netarsudil has a marketing authorisation for the reduction of elevated intraocular pressure (IOP) in adult patients with primary open-angle glaucoma or ocular hypertension. Netarsudil has been studied in randomised controlled trials compared with a beta-blocker, a prostaglandin analogue and placebo.

Intervention	Netarsudil
Population	Adults with primary open-angle glaucoma or ocular hypertension and elevated intraocular pressure
Comparators	Topical (eye drops), monotherapy or in combination: • Prostaglandin analogues (for example bimatoprost, latanoprost, tafluprost, travoprost) • Beta-blockers (for example betaxolol, carteolol hydrochloride, levobunolol hydrochloride, timolol maleate) • Carbonic anhydrase inhibitors (for example acetazolamide, brinzolamide, dorzolamide) • Sympathomimetics (for example apraclonidine, brimonidine tartrate) • Selective laser trabeculoplasty.

Outcomes	The outcome measures to be considered include: • mean intraocular pressure • visual acuity • visual field test • evaluation of anterior and posterior segment parameters • structural integrity of the optical nerve • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. Cost effectiveness analysis should include consideration of the benefit in the best and worst seeing eye.
Other considerations	If the evidence allows, consideration will be given to subgroups of people with OHT and people with COAG. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	**Appraisals in development (including suspended appraisals)** 'Glaucoma – lerdelimumab (CAT-152)' NICE technology appraisal [ID1383]. Suspended. **Related Guidelines** 'Glaucoma: diagnosis and management' (2017). NICE guideline NG81. Update in progress. Exceptional surveillance report of NICE guideline NG81. September 2019. **Related Interventional Procedures** 'Repetitive short pulse transscleral cyclophotocoagulation for glaucoma'. NICE interventional procedures guidance [ID1779]. Publication date to be confirmed.

	'High-intensity focused ultrasound for glaucoma' (2019). NICE interventional procedures guidance 661. 'Microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma' (2018). NICE interventional procedures guidance 612. 'Trabecular stent bypass microsurgery for open-angle glaucoma' (2017). NICE interventional procedures guidance 575. 'Ab extemo canaloplasty for primary open-angle glaucoma' (2017). NICE interventional procedures guidance 591. 'Trabeculotomy ab interno for open angle glaucoma' (2011) NICE interventional procedures guidance 397. **Related Quality Standards** 'Serious eye disorders' (2019). NICE quality standard QS180. **Related NICE Pathways** Glaucoma (2011, updated 2019) NICE pathway **NICE advice:** The SENSIMED Triggerfish contact lens sensor for continuous 24-hour recording of ocular dimensional changes in people with or at risk of developing glaucoma (2014) NICE MedTech innovation briefing 14. Glaucoma: brinzolamide/brimonidine combination eye drops (2015) NICE Evidence Summary New Medicines 56.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) Manual for prescribed specialised services 2018/19. Chapter 12 adult specialist ophthalmology services. Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 2 https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 Royal College of Ophthalmologists (2016) Commissioning guide: Glaucoma NHS England (2014) Improving eye health and reducing sight loss, a 'Call to Action' NHS England (2013) Local Eye Health Networks. Improving eye health and services. A Getting Started Guide NHS England (2013) Local Eye Health Networks. Improving eye health and services. A Getting Started Guide NHS England (2013) NHS standard contract for specialised ophthalmology (adult). Service specification number: D12/S/a

Questions for consultation

Have all relevant comparators for netarsudil been included in the scope? Are carbonic anhydrase inhibitors, sympathomimetics, combination treatments and SLT considered first-line or-second line treatments?

Which treatments are considered to be established clinical practice in the NHS for open angle glaucoma and ocular hypertension?

Where do you consider netarsudil will fit into the existing pathways for glaucoma?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom netarsudil is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which netarsudil will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider netarsudil to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of netarsudil can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal

processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1 King A, Azuara-Blanco A, Tuulonen A (2013) Glaucoma. The British Medical Journal 346: f3518. Accessed July 2020.

2 Horizon Scanning Research and Intelligence Centre (2017). Netarsudil plus latanoprost (Roclatan) for glaucoma or ocular hypertension. Accessed July 2020.

3 Moorfields Eye Hospital (2020) Glaucoma. Accessed July 2020.

4 Office of National Statistics (ONS) 2019 Mid-year population projections. Accessed July 2020.