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Health Technology Briefing
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Bimatoprost slow-release for ocular hypertension or open-angle glaucoma

Company/Developer	Allergan

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 7953	NICE ID: 10179	UKPS ID: 649154

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Bimatoprost slow-release (implant) is currently in clinical development for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma (OAG) or ocular hypertension (OHT) who are unsuitable for topical IOP-lowering medications. OHT occurs when the IOP of the eye is raised and can cause glaucoma if untreated. Although OHT is a big risk factor for OAG, OAG can be caused by a number of other risk factors including age, comorbidities and family history. OAG is the most common form of glaucoma, and it is caused by fluid build-up in the eye. If untreated, it can lead to vision loss. Treatment of OHT and/or OAG are typically topical medicines and/or selective laser trabeculoplasty (SLT). However, the main issue with topical medicines, although effective, is poor treatment adherence.

Bimatoprost slow-release is an ocular hypotensive agent designed to reduce IOP. It is being developed as intracameral injection to be administered into the eye and will be administered with a maximum of 2 implants within a 12-month period and a minimum retreatment interval of 4 months. Duration of treatment is being evaluated. In this way, bimatoprost slow-release has the potential to change glaucoma care by decreasing the challenge of medication adherence and also addressing the burden of disease for glaucoma patients. If approved, it will be the first slow release intracameral treatment in the UK; providing an alternative treatment option for patients with OHT or OAG that are unsuitable, or non-adherent to topical medications.

Proposed Indication

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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For the reduction of Intraocular Pressure (IOP) in patients with open-angle glaucoma (OAG) or ocular hypertension (OHT) who are unsuitable for topical IOP-lowering medications.[1,2]

Technology

Description

Bimatoprost slow-release biodegradable implant (Durysta, AGN-192024, bimatoprost sustained-release, bimatoprost SR) is a potent ocular hypotensive agent.[1,2] It is a synthetic prostamide, structurally related to prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), that does not act through any known prostaglandin receptors. Bimatoprost selectively mimics the effects of newly discovered biosynthesised substances called prostamides. The mechanism of action by which bimatoprost reduces IOP in humans is by increasing aqueous humour outflow through the trabecular meshwork and enhancing uveoscleral outflow.[3] Bimatoprost slow-release biodegradable implant is currently in clinical development for the reduction of IOP in patients with OAG or OHT who are unsuitable for topical medication.[1,2]

In the phase III trial (NCT02507687), the eye randomized to receive bimatoprost slow-release 10µg has received an intracameral administration of bimatoprost slow-release on day 4, plus sham selective laser trabeculoplasty (SLT) administration on day 1 only. Cycle 2 administration of bimatoprost slow-release was performed at week 16 for all patients who meet retreatment criteria.[2] For those patients not meeting retreatment criteria at week 16, cycle 2 may be performed at the investigator's discretion during an unscheduled visit after week 16 and prior to the month 12 visit if the retreatment criteria are met. Duration of treatment is being evaluated.[a,b]

Key Innovation

First-line treatment for OAG usually involves the use of topical IOP-lowering medications, most commonly prostaglandin analogues (PGAs). Although topical medications are generally efficacious in lowering IOP, adherence issues frequently complicate disease management. Factors reported to negatively impact adherence to topical IOP-lowering medications include a poor understanding of the disease, poor self-efficacy, difficulty in eye drop administration, forgetfulness, multiple dosing requirements, and adverse events.[4] As the standard of care for those patients with mild-moderate OHT and OAG who are unsuitable for topical medications is selective laser trabeculoplasty (SLT) which has limited repeatability, laser has been chosen as the comparator in the pivotal trial.[2,b]

Bimatoprost implant reduces IOP with a sustained effect in patients with OAG or OHT based on available data from two phase III US pivotal trials (NCT02247804 and NCT02250651). In clinical trials in patients with OAG or OHT, the intracameral bimatoprost implant had acceptable safety and tolerability after one administration and with the new clinical trials it is expected to show an acceptable safety profile with two administrations.[1,4,5] Bimatoprost slow-release drug delivery also has the potential to change glaucoma care by decreasing the challenge of medication adherence. It is currently the only FDA-approved slow-release intracameral treatment available. Clinical trials have shown that bimatoprost SR can provide comparable levels of IOP control as topical eyedrops. It has advantages such as decreasing concerns

[a] Information provided by Allergan

[b] Information provided by Allergan on UK PharmaScan

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regarding drop adherence, reducing ocular surface and periocular side effects from topical drops, and decreased daily treatment burden for patients.[6]

Regulatory & Development Status

Bimatoprost slow-release biodegradable implant does not currently have Marketing Authorisation in the EU/UK for any indication.

However, bimatoprost eye drops is licensed in the UK for the reduction of elevated IOP in chronic OAG and OHT in adults (as monotherapy or as adjunctive therapy to beta-blockers).[3]

Patient Group

Disease Area and Clinical Need

Glaucoma is a group of eye disorders characterised by a loss of visual field associated with pathological cupping of the optic disc and optic nerve damage. While glaucoma is generally linked to raised IOP, which is the main treatable risk factor, it can also occur when the IOP is within the normal range. Other risk factors include age, family history, ethnicity, corticosteroid use, myopia, type 2 diabetes mellitus, cardiovascular disease, and hypertension. The most common form of glaucoma is OAG.[7] OAG is a chronic and progressive eye disorder that is characterized by optic nerve damage and is commonly associated with elevated IOP. In OAG, disease progression leads to irreversible visual field loss and, if untreated, can result in blindness.[4] Patients with OHT (an IOP greater than 21 mmHg) are at high risk of developing primary OAG.[7]

OHT affects 3-5% of people in the UK over 40 years of age. Primary OAG affects about 2% of people in the UK older than 40 years.[8] The Royal College of Opthalmologists (RCO) predicts that from 2015 to 2035, the prevalence of the number of people in the UK with glaucoma will rise by 44% (22% rise from 2015 to 2025). This will be accompanied by a rise of 16% in the number with OHT.[9] The hospital episode statistics (HES) for diagnosis in England in 2020-2021, recorded a total of 7,678 finished consultant episodes (FCEs) for primary OAG (ICD-10: H40.1), resulting in a total of 478 admissions.[10]

Recommended Treatment Options

NICE recommends the following for the treatment of OHT:[11]

- Generic PGA for people with IOP of 24 mmHG or more, if they are at risk of visual impairment within their lifetime
- For people with OHT who are not at risk of visual impairment in their lifetime, they should continue regular visits to their primary eye care professional at clinically appropriate intervals
- For patients with IOP of 24 mmHg or more, who cannot tolerate their current treatment, the first choice should be an alternative generic PGA if available, and if this is not tolerated, offer a beta-blocker. If none of these options are tolerated, offer non-generic PGA, carbonic anhydrase inhibitors, sympathomimetics, miotics or a combination of treatments
- A drug from another therapeutic class (beta-blocker, carbonic anhydrase inhibitor[2] or sympathomimetic) to people with an IOP of 24 mmHg or more whose current treatment is not reducing IOP sufficiently to prevent the risk of progression to sight loss. Topical drugs from different therapeutic classes may be needed at the same time to control IOP.

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NICE recommends the following for the treatment of primary OAG:[12]

- Offer a generic PGA to people with primary OAG
- Offer people with advanced primary OAG, surgery with pharmacological augmentation (*mitomycin C*) as indicated.
- Offer people who present with advanced primary OAG and who are listed for surgery, interim treatment with a generic PGA.
- If adherence and eye drop instillation technique are satisfactory offer 1 of the following: a drug from another therapeutic class (a beta-blocker, carbonic anhydrase inhibitor or sympathomimetic), laser trabeculoplasty, surgery with pharmacological augmentation

Clinical Trial Information	
Trial	NCT02247804; 2014-003037-26; The Efficacy and Safety of Bimatoprost SR in Patients With Open-angle Glaucoma or Ocular Hypertension **Phase III:** Completed **Location(s):** 6 countries in EU (not including UK), USA and other countries **Primary completion date:** February 2018
Trial Design	Randomised, parallel assignment, quadruple-blinded
Population	N = 594 (actual); Diagnosis of either OAG or OHT in each eye and both eyes require IOP-lowering treatment; aged 18 years and older.
Intervention(s)	Bimatoprost SR, 10 µg
Comparator(s)	Timolol 0.5%
Outcome(s)	• Change From Baseline in IOP in the Study Eye at Week 12 (Hours 0 and 2) [Time frame: Baseline (hours 0 and 2) to week 12 (hours 0 and 2)] See trial record for full list of other outcomes
Results (efficacy)	See trial record
Results (safety)	See trial record

Clinical Trial Information	
Trial	NCT02507687; 2015-002131-18; A Comparison of Bimatoprost SR to Selective Laser Trabeculoplasty in Patients With Open-Angle Glaucoma or Ocular Hypertension **Phase III:** Active, not recruiting **Location(s):** 4 countries in EU, UK, USA, Canada and other countries. **Primary completion date:** May 2023
Trial Design	Randomised, parallel assignment, quadruple-blinded
Population	N = 215; Diagnosis of either OAG or OHTin each eye that require IOP lowering treatment; aged 18 years and older.

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Intervention(s)	Up to 2 bimatoprost SR adminsitrations
Comparator(s)	Selective laser trabeculoplasty
Outcome(s)	• Change from Baseline in IOP at week 4 [Time frame: Baseline, Week 4] • Change from Baseline in IOP at week 12 [Time frame: Baseline, Week 12] • Change from Baseline in IOP at week 24 [Time frame: Baseline, Week 24]
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of bimatoprost SR is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Netarsudil for treating open angle glaucoma or ocular hypertension (ID1078). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Netarsudil-latanoporst for previously treated open angle glaucoma or ocular hypertension (ID1363). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Glaucoma - lerdelimumab (CAT-152) (ID383). Expected date of issue to be confirmed.
- NICE guideline in development. Glaucoma: diagnosis and management (GID-NG1020). Expected date of issue January 2022.
- NICE guideline. Glaucoma: diagnosis and management (NG81). November 2017.
- NICE quality standard. Serious eye disorders (QS180). February 2019.
- NICE interventional procedure. Repetitive short-pulse transscleral cyclophotocoagulation for glaucoma (IPG692). April 2021.
- NICE interventional procedure guidance. Microinvasive subconjunctival insertion of a trans-scleral gelatin stent for primary open-angle glaucoma (IPG612). April 2018.
- NICE interventional procedure guidance. Ab externo canaloplasty for primary open-angle glaucoma (IPG591). September 2017.
- NICE interventional procedure guidance. Trabecular stent bypass microsurgery for open-angle glaucoma (IPG575). February 2017
- NICE interventional procedure guidance. Trabeculotomy ab interno for open angle glaucoma (IPG397) May 2011.

NHS England (Policy/Commissioning) Guidance

NHS England. 2013/14 NHS Standard Contract for Specialised Ophthalmology (Adult). D12/S/a.

Other Guidance

- European Glaucoma Society. Terminology and Guidelines for Glaucoma. March 2017.[13]
- Clinical Council for eye health commissioning: the Royal College of Ophthalmologists. Commissioning guide: Glaucoma (recommendations). June 2016.[14]
- Scottish Intercollegiate Guidelines Network (SIGN). Glaucoma referral and safe discharge (SIGN144). March 2015.[15]

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Additional Information

Additional clinical trials that may be used to support regulatory/Health Technology Assessment (HTA) submission by the company include: NCT02250651, NCT02636946, NCT03891446, NCT04285580, NCT03850782.[5,16-19]

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