Nye metoder - Request for assessment of medicinal product

To request an assessment of a new medicinal product or a new indication for an existing medicinal product through Nye metoder, health technology developers should complete this form. By submitting a request for assessment, the developer signals that it plans to submit documentation for such an assessment.

Please send the completed form to Nye metoder by e-mail: nyemetoder@helse-sorost.no.

A request for assessment may not be submitted prior to day 120 of the European Medicines Agency (EMA) marketing authorisation assessment process for new medicinal products under regular approval procedure, or prior to day 1 for variation/extension assessments and for medicinal products under accelerated assessment.

This form must be completed in its entirety. Nye metoder will plan the assessment process based on the information provided in the request form.

At the time of request for assessment, the health technology developer must have a plan for when it intends to submit documentation for assessment.

Information about Nye metoder can be found online (nyemetoder.no). Please contact Sekretariatet for Nye metoder if you have any questions.

Please note: The form will be published in its entirety.

The submitter is aware that the form will be published in its entirety (**tick**): ☑

1 Contact information	
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2 Medicinal product overview

Does the request concern a new active substance?	No, a new administration form of exciting active compound and a new brand name
Trade name	Durysta
Generic name	Bimatoprost intracameral implant (Bimatroprost intrakameralt implantat)
Marketing authorisation in Norway	Abbvie A/S
ATC code	S01EE03
Mode of administration	Intracameral implant containing 10 µg of bimatoprost preloaded in a single use applicator.
Pharmacotherapeutic group and mechanism of action *Briefly describe*	Prostaglandin. Bimatoprost lowers IOP (intraoccular pressure) by increasing outflow of aqueous humour through both the trabecular meshwork and uveoscleral pathways. The biodegradable Durysta implant provides a non-pulsatile, continuous release of bimatoprost over a 3–4-month period, with drug delivery targeted to the iris-ciliary body. This targeted delivery method enables a reduction of IOP (intraoccular pressure) by increasing the aqueous humour outflow directly in the conventional and unconventional fluid pathways.
Expected indication relevant to the request *Expected indication must be written in Norwegian*	DURYSTA er indisert for reduksjon av intraokulært trykk (IOP) hos voksne med åpenvinklet glaukom (OAG) eller okulær hypertensjon (OHT) som er uegnet for topiske IOP-senkende medisiner.

3 Assessment history

Has the medicinal product previously been assessed by Nye metoder for other indications? *If yes, enter the Nye metoder ID number*	No
Are you aware of other medicinal products assessed by Nye metoder for the same indication? *If yes, enter the Nye metoder ID number*	No other evaluations for pharmaceuticals have been performed for this indication. However, an evaluation of Minimally Invasive Glaucoma Surgery (MIGS) for individuals with Glaucoma was performed in 2021. ID: ID2018_072.

4 Expected timeline	
Procedure number for the marketing authorisation assessment in EMA	EMEA/H/C/005916/0000
Expected date (month/year) of CHMP positive opinion	Feb 2024
Expected date (month/year) of marketing authorisation in Norway	April 2024
Expected date (quarter/year) for submission of documentation to Norwegian Medicines Agency *Dates must be stated*	Q1 2024

5 Diagnostics and resource use Fill inn where relevant	
Will the new method require diagnostic testing for biomarker analysis?	No
Which biomarker(s) are relevant and which publications describe this? *Please refer to publications*	N/A
Do you know whether diagnostics can be performed by the public health service or whether it must be performed by an external supplier?	All test and procedures can be carried out in the public service
Will introduction of the new method require establishment of other/new infrastructure? *For example, custom analysis machine, digital pathology/ AI-based analysis, proteomics, functional tests etc.?*	No, Implantation of Durysta® is minimally invasive and can be undertaken in standard aseptic conditions for intracameral procedures which is common.
Pre-analytical requirements *For example, biopsies, other sampling, sample processing etc. are required.*	No

Test execution: is there a need to establish one specific test or is a biomarker already established in the health service (e.g. in gene panels)?	No
Description of reading of results including data analysis program if necessary.	N/A
Which patient groups need to be tested, and what is the expected proportion of findings that provide treatment options?	N/A

6 Description of the disease and current treatments

Description of the disease *<u>Brief</u> description of the pathophysiology and clinical presentation/symptoms, possibly including references*	Glaucoma is the main cause of irreversible blindness in the world. Open-angle glaucoma is the most common type of glaucoma. Frequently presents asymptomatically and can be identified on routine ophthalmic examination. Intraocular pressure is most often elevated, but may be normal in some cases. Optic disk cupping is diagnostic. Glaucoma is a neurodegenerative condition primarily due to dysfunction in outflow of aqueous humor, the nutrient-rich fluid that constantly flows through the eye. Aqueous humor, created in the ciliary body, passes through the pupil into the small area between the iris and the cornea, called the anterior chamber. The fluid then flows into the periphery of the chamber known as the anterior chamber angle. This angle is where the fluid travels through the trabecular meshwork and into blood vessels. Open-angle glaucoma is characterized by an anatomically open angle but with an obstructed and slowed drainage system outflow. The mechanism of blockage is unclear. An increase in intraocular pressure results, characterized by retinal ganglion cell damage, then peripheral vision loss in early disease and central vision loss in late disease. Referanse: British Medical Journal (https://bestpractice.bmj.com/topics/en-us/373)
Therapeutic area *Specify which field best describes the method*	Radiologi og nukleærmedisin Sykdommer i nyrer, urinveier og kjønnsorganer Øre-, nese- og halssykdommer **Øyesykdommer**
Cancer *If the method applies to the medical field of cancer, specify which type of cancer is relevant*	*** Ingen Kreftsykdom** Bein- og bløtvevskreft Blod- beinmargs- og lymfekreft Brystkreft Mage- og tarmkreft
Current treatment *Current standard treatment in Norway, including references*	There is no curative treatment for glaucoma and vision loss from glaucoma is irreversible. The objective of glaucoma management is to provide a significant and sustained decrease in intraocular pressure (IOP) which minimises the risk of progression (i.e. visual field loss) and preserves a patient's quality of life. All glaucoma treatments have potential side effects or complications. Thus, when making the choice of a treatment or providing additional treatment, the overriding consideration must be to minimise the risks and maximise the benefits to patients. Initial therapy for most forms of glaucoma is topical medication with IOP lowering eye drops, either as monotherapy or in combination with other eye drops with different mechanisms of action. However, topical medications are not suitable for some patients due to challenges adhering to difficult regimes, difficulties with administration and side effects that may create significant hurdles to achieve adequate control of eye pressure. Non-adherence is specifically a concern in managing IOP, it can result in large IOP fluctuations, which are associated with an increased risk of vision loss. For patients who are not suitable for, have inadequate effect and or do not tolerate topical medication, the next option is usually laser surgery (Selective laser trabeculoplasty – SLT). SLT is a short procedure but is not recommended for some patients with glaucoma because of contraindications. The efficacy of SLT has also shown to be unpredictable (ref. klinikerinnspill ID2018_072) After topical medication and SLT, the current remaining options are surgical methods. In 2021, minimally invasive glaucoma surgery (MIGS) was approved by Decision forum for the treatment of Glaucoma in Norway. MIGS represents a class of various surgical procedures and devices that aims to provide a minimally invasive surgical treatment option that reduces IOP while limiting damage to conjunctiva. For more severe cases or if no other treatment options are available, the last resort is more invasive surgery that provides an alternate drainage for the eye fluid, thus lowering IOP. The downside of these

Prognosis *Describe the prognosis with current treatment options, including references*	Glaucoma is a chronic disease and patients will need treatment for the rest of their life. It will progress over time and can result in vision loss. Glaucoma therapy can prevent or postpone the progression of disease. Early identification, early treatment initiation and good treatment adherence are important for maintaining vision and slowing down progression. Ref: https://www.helsenorge.no/sykdom/oyesykdommer/glaukom/#prognose
The new medicinal product's placement in the treatment algorithm	Non-adherence, tolerance issues, lack of efficacy and contraindications are key issues for patients treated with eye drops and laser treatments today. Durysta is expected to be a treatment alternative for patients who are not physically or mentally able to handle drops, who do not tolerate drops or have inadequate efficacy on drops, and for patients who are not suitable for laser surgery
Patient population *Description, incidence and prevalence of the patient population covered by the relevant indication* in Norway, including references.* *Number of Norwegian patients assumed to be relevant for new method* ** The entire patient group covered by the indication in question is to be described*	The indication for the new intracameral slow-release version of bimatoprost, is for patient unsuitable for drop treatment. Patients considered unsuitable for drop treatment would be patients with shown or expected lack of adherence to regular topical drop treatment or are intolerant to drop treatment. Reasons for lack of adherence could be treatment limiting diagnoses such as Dementia, Rheumatoid Arthritis and/or other physically or mentally debilitating diagnoses. Other reasons could be adherence issues based on drop related adverse events. Pain, stinging, burning sensation, cases of Ocular Surface Disease (OSD). In total, 75733 patients were treated with IOP-lowering eyedrops in Norway in 2018. The national, age irrespective, glaucoma prevalence in Norway in 2018 was 1.4% (men 1.3%, women 1.6%), while for those over 50 years of age it was 3.7% (men 3.5%, women 4.0%), and for those 70 years and over, 8.0% (men 7.6% and women 8.6% respectively) . In 2018 there were 9034 (4537 men, 4497 women) new patients treated for glaucoma. The incidence proportion of glaucoma was slightly higher in males than females in each age group above 50 years. This difference was significant in the age groups 70–79, 80–89, and 90+ ($p<0.01$). Durysta will be a treatment alternative for patients who are unsuitable for eye drops, expected to 8-10% (AbbVie estimate) of patients treated for glaucoma with topical medication and SLT. Reference: 1. Slettedal JK, Traustadóttir VD, Sandvik L, et al. The prevalence and incidence of glaucoma in Norway 2004-2018: A nationwide population-based study. PLoS One. 2020 Dec 10;15(12):e0242786.

7 Comparability to other medicinal products and inclusion in tender

Are there existing procurements or tenders in the therapeutic area?	No
Are there other medicinal products with a similar mechanism of action and/or similar effect (for the same indication)?	Durysta is a novel treatment for glaucoma, with bimatoprost as the active ingredient. It is implanted into the anterior chamber and is slow-release implant with continuous release of bimatoprost over a 3–4-month period. Bimatoprost is currently used as a topical treatment for glaucoma, along with other prostaglandin analogues.
Does the supplier consider the medicinal product to be comparable to other medicinal products?	Clinical efficacy comparable to topical drops and SLT, but Durysta is relevant for the patient population unsuitable for eye drops and laser surgery.

8 Relevant clinical trials
(pivotal trial(s) and clinical studies relevant for establishing relative efficacy)

	Study 1	Study 2	Study 3
Study ID *Study name, NCT number, hyperlink*	APOLLO: Phase 1/2 Study Design ClinicalTrials.gov Identifier: NCT01157364.	ARTEMIS 1&2: Phase 3 Study Design ClinicalTrials.gov Identifiers: NCT02247804 and NCT02250651.	Athena 1&2, Phase 3 Study design. ClinicalTrials.gov Identifiers: NCT02507687.
Study type and design	This was a phase 1/2, prospective, 24-month, dose-ranging, paired-eye trial in patients with open-angle glaucoma.	Randomized, 20-month, multicenter, subject- and efficacy evaluator-masked, parallel-group, phase 3 clinical studies	This study is a multicenter, paired-eye, randomized, efficacy evaluator-masked 26-month study conducted in 2 stages and evaluating 2 different dose strengths of Bimatoprost SR (Stage 1: 15 µg; Stage 2: 10 µg).
Objective	The Objective of This Study Was to Evaluate the Safety and IOP-Lowering Effects Over 24 Months of Biodegradable Bimatoprost Sustained-Release Implant Administration Versus Topical Bimatoprost 0.03% In Patients With OAG	The Objective of these Studies Was to Evaluate the Efficacy and Safety of Bimatoprost Implant in Comparison With Topical Timolol for Lowering IOP in Subjects With OAG or OHT	To evaluate the intraocular pressure (IOP)-lowering effect and safety of Bimatoprost SR compared with selective laser trabeculoplasty (SLT) in patients with open-angle glaucoma (OAG) or ocular hypertension (OHT) who are not adequately managed with topical IOP-lowering medication for reasons other than medication efficacy (eg, due to intolerance or nonadherence)
Population *Important inclusion and exclusion criteria*	Key inclusion criteria: IOP 22 to 36 mm Hg after washout Open angle qualified by clinical gonioscopy and via OCT	Key inclusion criterias: Open angle qualified by clinical gonioscopy (earlier patients qualified via OCT) IOP in both eyes 22–32 mm Hg after washout Key exclusion criteria included history of anatomically narrow angle that resulted in evidence of angle changes, or history of closed-angle glaucoma in either eye; subject nonresponsive to topical ophthalmic beta-blockers and/or PGAs;	Key inclusion criteria: Open angle qualified by clinical gonioscopy (earlier patients qualified via OCT) IOP in both eyes 22–34 mm Hg after washout
Intervention (n) *Dosage, dosing interval, duration of treatment*	After washout of previous IOP-lowering medication, patients received an intracameral injection of Bimatoprost SR (6-, 10-, 15-, or 20-µg formulation) in the study eye	Study eyes in the bimatoprost implant groups received implant on administration day visits (day 1, week 16, and week 32) and vehicle eye drops BID for masking	Patients will receive an administration of Bimatoprost SR on Day 4, with a repeat administration of Bimatoprost SR at Week 16 if the patient meets the retreatment criteria.
Comparator (n) *Dosage, dosing interval, duration of treatment*	In parallell to the intracameral injection in the study eye, treatment was initiated with once-daily topical bimatoprost 0.03% in the fellow eye. Rescue topical IOP-lowering medication was allowed in either eye, and a second treatment with Bimatoprost SR was allowed in the study eye between day 90 (week 12 is an approximation) and month 12.	Study eyes in the timolol group received topical timolol maleate 0.5% (timolol) BID and a sham procedure on administration day visits for masking.	Patients will receive a 360° administration of SLT in 1 eye on Day 1 (In order to mask the patient to the treatment assigned to each eye, on Day 1, a sham SLT procedure will be performed in the eye that will receive Bimatoprost SR administrations)
Endpoints *Primary, secondary and exploratory endpoints, including definition, measurement method and, if applicable, time of measurement*	Primary efficacy endpoint: Change from baseline in IOP Other measures: Safety parameters and the use of rescue medication	Primary efficacy endpoint: Mean Change in IOP from Baseline Through Week 12 (ITT Population). Key secondary endpoints: IOP between 12 weeks and 12 months	Primary efficacy analysis: Noninferiority to SLT during primary efficacy period (week 24). Key secondary endpoints: IOP between 24 weeks and 24 months
Relevant subgroup analyses *Description of any relevant subgroup analyses*	N/A	N/A	N/A

	Study 1	Study 2	Study 3
Follow up time *If the study is ongoing, indicate the follow-up time for the data expected to be available for assessment by the Norwegian Medicines Agency as well as the expected/planned total follow-up time for the study*	24 months (see above)	20 months (see above)	26 months (see above)
Time perspective results *Ongoing or completed study? Available and future data cut-offs*	Completed	Completed	Completed
Publications *Title, author, journal, year. Expected date of publication*	Craven ER, et al. Drugs. 2020;80(2):167-179.	Medeiros FA, et al. Ophthalmology. 2020;127 (12):1627-1641. J. Bacharach et al. Drugs https://doi.org/10.1007/s40265-021-01624-9	Not published yet

9 Ongoing and planned studies

Are there ongoing or planned studies for the medicinal product within the same indication that may provide further information in the future? *If yes, state the expected time perspective for data availability*	TRITON A Phase 3b Study to Evaluate the Duration of Effect of Bimatoprost SR in Participants with Open-Angle Glaucoma or Ocular Hypertension Phase 3b study to evaluate the duration of intraocular pressure (IOP)-lowering effect and safety of up to three pro re nata (PRN) administrations of 10 µg Bimatoprost sustained release (SR) in the study eye of participants with open-angle glaucoma (OAG) or ocular hypertension (OHT) who are not adequately managed with topical IOP-lowering medication for reasons other than medication efficacy (eg, due to intolerance or nonadherence). NCT03850782 ARGOS A Phase IV, Prospective, 18-month Study to Assess the Effectiveness and Safety of Bimatoprost Intracameral Implant (DURYSTA) in US Clinical Practice NCT04647214
Are there ongoing or planned studies for the medicinal product for other indications?	No

10 Expected health economic documentation

Enter information about the expected health economic analysis

Type of health economic analysis *E.g. cost-per-QALY analysis or cost minimisation analysis* *(Justify the proposal)*	"Förlöp B: Vurdere om det er sammenlignbar effekt og sikkerhet mellom nytt og etablert legemiddel. Denne typen metodevurdering vil til forskjell fra «konkurranseutsetting» også inneholde vurdering av relativ effekt." Durysta has clinical equal efficacy compared to topical IOP lowering drops and SLT
The patient population on which the health economic analysis is based, including any subgroups. *The main analysis (base case) shall include the entire patient population covered by the indication sought.*	N/A
What type of documentation will form the basis for estimating relative efficacy? *(Direct or indirect evidence)*	H2H vs drops H2H vs selective laser trabeculoplasty (SLT)
What type of documentation will form the basis for health-related quality of life data?	N/A
Expected pharmaceutical budget impact per year, in the 5-year period following a potential approval	Will be included in application

11 Suitable for FINOSE?

Can the method be appropriate for assessment through FINOSE (yes/no) *If no, why not?*	No

12 Other relevant information

Disclose other aspects that Nye metoder should be aware of.

Have you been in contact with clinicians at Norwegian health trusts about this medicinal product/ indication? Yes/no *If so, who have you been in contact with and what have been their contribution?* *(Relevant information in connection with the recruitment of experts in the field at Nye metoder)*	Yes Olav Kristianslund at OUS
Are there specific circumstances related to the medicinal product implying that a plain discount may not be appropriate for fulfilment of the priority criteria (yes/no)? *If yes, a separate form must be completed and sent nyelegemidler@sykehusinnkjop.no at the same time as documentation is sent to the Norwegian Medicines Agency for a health technology assessment.* *Information and form:* https://www.sykehusinnkjop.no/om-oss/informasjon-og-opplering/	No
Any other relevant information?	AbbVie would like a pre-meeting to discuss the process and the submission documentation when request from Bestillerforum is ready.