Gemeinsamer Bundesausschuss

Justification

of the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive: Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a (SGB V) Latanoprost/Netarsudil (reduction of elevated intraocular pressure in open-angle glaucoma or ocular hypertension, pretreated)

of 15 June 2023

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of reimbursable medicinal products with new active ingredients. This includes in particular the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical trials the pharmaceutical company has conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirements for a quality-assured application.

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decides on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The relevant date for the start of the benefit assessment procedure was the first placing on the (German) market of the combination of active ingredients latanoprost/ netarsudil on 15 December 2022 in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA. The pharmaceutical company submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 1 VerfO on 9 December 2022.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 15 March 2023 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of latanoprost/ netarsudil compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG and

the statements submitted in the written statement and oral hearing procedure (as well the addendum drawn up by the IQWiG on the benefit assessment). In order to determine the extent of the additional benefit, the G-BA has evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5, Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of latanoprost/ netarsudil.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA has come to the following assessment:

2.1 Additional benefit of the medicinal product in relation to the appropriate comparator therapy

2.1.1 Approved therapeutic indication of latanoprost/netarsudil (Roclanda) according to the product information

Roclanda 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.

Therapeutic indication of the resolution (resolution of 15.06.2023):

See the approved therapeutic indication.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with primary open-angle glaucoma or ocular hypertension for whom monotherapy with a prostaglandin or netarsudil provides insufficient IOP reduction

Appropriate comparator therapy:

Combination therapy of beta-blocker + prostaglandin analogue or prostamide as free or fixed combination

Criteria according to Chapter 5, Section 6 of the Rules of Procedure of the G-BA:

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication in accordance with the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5, Section 6, paragraph 3 VerfO:

[1] General Methods, version 6.1 from 24.01.2022. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

Justification based on the criteria set out in Chapter 5, Section 6, paragraph 3 VerfO:

on 1. For the treatment of elevated intraocular pressure in the case of open-angle glaucoma or ocular hypertension, in addition to the combination of active ingredients latanoprost/ netarsudil, a variety of approved medicinal products that increase aqueous humour outflow or reduce aqueous humour production are available. These include medicinal products belonging to the following product classes and the following active ingredients:

- Beta-blockers (betaxolol-HCl, carteolol, levobunolol, metipranolol, timolol)
- Alpha 2 sympathomimetics (brimonidine, clonidine)
- Carboanhydrase inhibitors (acetazolamide (oral, parenteral), brinzolamide, dorzolamide)
- Parasympathomimetics (carbachol, pilocarpine)
- Prostaglandin analogues or prostamides (bimatoprost, latanoprost, tafluprost, travoprost)
- Rho-kinase inhibitors (netarsudil[2])

on 2. Alternative treatment approaches such as laser surgery (e.g. Laser trabeculoplasty) or surgical procedures (e.g. trabeculectomy, trabeculotomy, cryocoagulation or photocoagulation of the ciliary body) are generally only considered after failure of medicinal therapy or compelling contraindications.

on 3. In the present therapeutic indication, there is a resolution of the Federal Joint Committee on the benefit assessment of active ingredients according to Section 35a SGB V of 18 June 2015 for the combination of active ingredients tafluprost/ timolol.

on 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V".

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the

[2] Approved for the treatment of primary open-angle glaucoma or ocular hypertension, but not available in Germany.

comparator therapy in the present therapeutic indication according to Section 35a, paragraph 7 SGB V.

The aim of medicinal therapy for elevated intraocular pressure in the case of open-angle glaucoma or ocular hypertension is to prevent optic nerve damage, i.e. to maintain vision at a constant level of quality. This is to be achieved by lowering the intraocular pressure to the "patient-individual target pressure". In addition to the treatment of risk factors that influence the course of the disease, such as diabetes mellitus or hypertension, patient training in the correct use of eye drops or the like, as well as further steps to improve patient adherence are recommended as additional supportive measures to achieve the therapeutic goal.

Due to the approved therapeutic indication of latanoprost/ netarsudil, this combination of active ingredients is an alternative treatment for patients in whom the individual therapeutic goal has not yet been achieved with hypotensive monotherapy using prostaglandins or netarsudil. Therefore, a combination therapy of beta-blocker + prostaglandin analogue or prostamide as a free or fixed combination was determined as the appropriate comparator therapy for adults with primary open-angle glaucoma or ocular hypertension for whom monotherapy with a prostaglandin or netarsudil provides insufficient IOP reduction. Thus, the other product classes approved for the treatment of open-angle glaucoma or ocular hypertension are to be considered as being excluded. Furthermore, according to the criteria for determining the appropriate comparator therapy, this is determined independently of the dosage form of the approved proprietary medicinal product and the excipients contained therein (e.g. preservatives). Thus, no distinction is made between preservative-containing and preservative-free medicinal products, so that the appropriate comparator therapy includes both preservative-containing and preservative-free combinations of the named classes of medicinal products.

The findings in Annex XII do not restrict the scope of treatment required to fulfil the medical treatment mandate.

A change in the appropriate comparator therapy requires a resolution by the G-BA linked to the prior review of the criteria according to Chapter 5, Section 6, paragraph 3 Rules of Procedure.

2.1.3 Extent and probability of the additional benefit

In summary, the additional benefit of latanoprost/ netarsudil is assessed as follows:

For the treatment of adults with primary open-angle glaucoma or ocular hypertension for whom monotherapy with a prostaglandin or netarsudil provides insufficient IOP reduction, an additional benefit of latanoprost/ netarsudil over bimatoprost/ timolol has not been proven.

Justification:

For the benefit assessment, the pharmaceutical company presents the MERCURY 3 study.

The MERCURY 3 study is a randomised, double-blind, parallel-group study in which the fixed combination of latanoprost and netarsudil was compared in a ratio of 1: 1 with the fixed combination of bimatoprost and timolol. 430 adult patients with primary open-angle glaucoma and/or ocular hypertension in both eyes treated with local hypotensive ophthalmic medication were enrolled in the study. The patients were inadequately controlled by their current monotherapy and/or, in the opinion of the principal investigator, there was a need for

combination therapy. Following two qualification visits, one eye was selected as the eye under study. If both eyes were eligible, the eye with the higher intraocular pressure at the start of the study was defined as the eye under study.

Since patients with any previous hypotensive therapies were enrolled in the MERCURY 3 study, its inclusion criteria were broader with regard to the patients' previous therapies than the specifications for the use of latanoprost/ netarsudil according to the product information. However, patients who had previously been treated with netarsudil were not enrolled in the study because netarsudil was approved in the European Union only after the start of the study.

The treatment duration was 180 days, with both eyes treated. The use of latanoprost/ netarsudil or bimatoprost/ timolol was in compliance with the marketing authorisation.

The primary endpoint of the MERCURY 3 study was mean intraocular pressure (IOP) within a treatment group at different time points up to month 3. The reduction of elevated intraocular pressure in the case of open-angle glaucoma or ocular hypertension is an important therapeutic goal for the prevention of disease-related secondary damage (e.g. optic nerve damage).

Patient-relevant secondary endpoints were endpoints on morbidity and health-related quality of life as well as adverse events (AEs).

The pharmaceutical company submits data for various subgroups, including patients with prostaglandin monotherapy prior to enrolment in the study. This sub-population corresponds to the relevant therapeutic indication according to the product information. The benefit assessment of latanoprost/ netarsudil therefore uses the data from the MERCURY 3 study for the sub-population with pretreatment with prostaglandin monotherapy. This sub-population comprises a total of 211 patients.

Extent and probability of the additional benefit

Mortality

In the MERCURY 3 study, no deaths occurred in the relevant sub-population in either study arm.

Morbidity

Restriction of the visual field

In the MERCURY 3 study, the visual field was determined using automated threshold value perimetry. The pharmaceutical company presents evaluations of the mean change at month 6 in the dossier.

In the diagnosis and follow-up of primary open-angle glaucoma or ocular hypertension, as well as for the treatment decision, the monoocular visual field is usually determined for the affected eyes. Visual field defects usually do not occur at corresponding points in both visual fields and are therefore compensated for by the perception of the other eye. Therefore, patients often notice visual field defects late or not at all, especially from the worse eye. According to the European Glaucoma Society guideline, visual impairment and thus, quality of life is largely determined by the binocular visual field or the visual field of the better eye. The evaluation of the binocular visual field would therefore be more suitable to detect perceptible or symptomatic visual impairments for the patient. Furthermore, the pharmaceutical company does not make any statements on the changes in the visual field which are to be

assessed as relevant and lead to noticeable changes for patients. There are no standardised threshold values in the guidelines that can be assessed as response or progression.

The evaluations presented for the endpoint of visual field limitation are not used for the derivation of the additional benefit, as no evaluations of the binocular visual field are available.

Best corrected visual acuity

The best corrected visual acuity in the study was measured using ETDRS-standard eye charts at a distance of 3 to 6 metres. An eye chart consists of 14 lines of optotypes, each with 5 letters, and thus, made up of a total of 70 letters. The size of the letters decreases with each line.

The pharmaceutical company presents evaluations of the mean change at month 6 as well as responder analyses of the improvement and deterioration of visual acuity in both eyes. In the present indication, deterioration of visual acuity may occur due to progression of the disease. An improvement in visual acuity could be due to decreasing intraocular pressure and thus, a better physiological function of the eye. Therefore, in the present indication, the evaluations for both improvement and deterioration of the best corrected visual acuity are considered.

For the endpoint of best corrected visual acuity, no statistically significant difference was detected between the treatment groups.

Health status (NEI VFQ-25, general health status sub-scale)

The NEI VFQ-25 is a questionnaire for measuring visual acuity-related quality of life, consisting of a total of 26 items and 12 sub-scales. Of these, 25 items (11 sub-scales) ask about vision and 1 item (1 sub-scale) about general health. The sub-scale on general health status is assigned to the morbidity category.

The pharmaceutical company presents both pre-specified evaluations of the mean change at month 6 and post-hoc responder analyses of the change in the sum score of the NEI VFQ-25 and the 12 sub-scales by 15% each.

By its statement, the pharmaceutical company also submits separate evaluations of the responder analyses for improvement and deterioration. These responder analyses are used for the benefit assessment.

For the endpoint of health status, there is no statistically significant difference between the treatment groups.

<u>Quality of life</u>

NEI VFQ-25 (sum score)

The NEI VFQ-25 is a questionnaire for measuring visual acuity-related quality of life, consisting of a total of 26 items and 12 sub-scales. Of these, 25 items (11 sub-scales) ask about vision and 1 item (1 sub-scale) about general health. The sub-scale on general health is assigned to the morbidity category.

The values of all items are transformed to a score from 0 to 100 and a score averaged over the items of the sub-scale is calculated for each sub-scale. The sum score finally results from the mean of the averaged scores of the sub-scales. The subscale on general health is not included

here. The sum score of the NEI VFQ-25 can take values between 0 and 100, with higher values indicating a better visual acuity-related quality of life.

The pharmaceutical company presents both pre-specified evaluations of the mean change at month 6 and post-hoc responder analyses of the change in the sum score of the NEI VFQ-25 and the 12 sub-scales by 15% each.

By its statement, the pharmaceutical company also submits separate evaluations of the responder analyses for improvement and deterioration. These responder analyses are used for the benefit assessment.

In the responder analyses, analogous to the evaluations of the mean change at month 6, there is no statistically significant difference between the treatment groups.

SF-36 (physical and mental component summary score)

The pharmaceutical company presents pre-specified evaluations of the mean change at month 6 and post-hoc responder analyses for the physical component summary (PCS) score and the mental component summary (MCS) score. For the responder analyses, the pharmaceutical company presents results for the response criterion of 15%, which corresponds to a change of 9.4 points (PCS) and 9.6 points (MCS). It describes the results shown as a change from the baseline value.

By its statement, the pharmaceutical company also submits separate evaluations of the responder analyses for improvement and deterioration. These responder analyses are used for the benefit assessment.

In the responder analyses, analogous to the evaluations of the mean change at month 6, there is no statistically significant difference between the treatment groups.

<u>Side effects</u>

By its statement, the pharmaceutical company submits missing data on side effects in the relevant sub-population.

Discontinuation due to AEs

For the endpoint of discontinuation due to AEs, there is a statistically significant difference between the treatment groups to the disadvantage of latanoprost/ netarsudil.

Subsequent documents from the pharmaceutical company indicate that only 1 of the 18 events in the latanoprost/ netarsudil arm was classified as serious. The event in the bimatoprost/ timolol arm was classified as not serious.

Ocular AEs

For the endpoint of ocular AEs, there is a statistically significant difference between the treatment groups to the disadvantage of latanoprost/ netarsudil. However, the documents submitted by the pharmaceutical company indicate that the most frequently occurring events are predominantly asymptomatic events that often do not affect the patients.

SAEs

For the endpoint of SAEs, no statistically significant difference was detected between the treatment groups.

Ocular SAEs

For the endpoint of ocular SAEs, no statistically significant difference was detected between the treatment groups.

Overall assessment

The assessment of the additional benefit is based on the randomised, double-blind MERCURY 3 study. The data for the sub-population with pretreatment with prostaglandin monotherapy were used for the benefit assessment of latanoprost/ netarsudil.

In addition to the negative effect in the endpoint of discontinuation due to AEs, there is also a negative effect in the endpoint of ocular AEs. However, the most common events are predominantly asymptomatic events that often do not affect patients. In the overall assessment of the available results, the negative effects in the endpoints of discontinuation due to AEs and ocular AEs are insufficient to infer a minor benefit of latanoprost/ netarsudil.

Overall, an additional benefit of latanoprost/ netarsudil compared with the appropriate comparator therapy bimatoprost/ timolol for adults with primary open-angle glaucoma or ocular hypertension for whom monotherapy with a prostaglandin or netarsudil provides insufficient IOP reduction is not proven.

Reliability of data (probability of additional benefit)

The assessment of the additional benefit is based on the randomised, double-blind MERCURY 3 study. Here, the data for the sub-population with pretreatment with prostaglandin monotherapy are used for the benefit assessment of latanoprost/ netarsudil.

Due to the high number of protocol deviations, whose extent of influence on the results of the MERCURY 3 study remains unclear, the cross-endpoint risk of bias of the study is assessed as high. This also results in a high risk of bias in the results for all endpoints of the study.

For the endpoints of health status (NEI VFQ-25) and health-related quality of life (NEI VFQ-25 and SF-36), there is also a high percentage of missing values, which also contributes to the high risk of bias of the results for these endpoints. For the endpoint of best corrected visual acuity, significantly different percentages of non-responder replacements between treatment arms contribute to the high risk of bias in the results.

The reliability of data of the study results is therefore reduced overall.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Roclanda with the combination of active ingredients latanoprost/ netarsudil.

Latanoprost/ netarsudil is indicated in the treatment of adults with primary open-angle glaucoma or ocular hypertension for whom monotherapy with a prostaglandin or netarsudil provides insufficient IOP reduction.

The G-BA determined a combination therapy of beta blocker + prostaglandin analogue or prostamide in a free or fixed combination as an appropriate comparator therapy.

For the assessment of the additional benefit, the pharmaceutical company submits the randomised, double-blind MERCURY 3 study. Here, the data for the sub-population with pretreatment with prostaglandin monotherapy are used for the benefit assessment of latanoprost/ netarsudil.

In the MERCURY 3 study, no deaths occurred in the relevant sub-population in either study arm. In the morbidity category, no statistically significant difference could be derived between latanoprost/ netarsudil and bimatoprost/ timolol in the change in best corrected visual acuity as well as in health status.

Also in the quality of life category, there is no statistically significant difference between latanoprost/ netarsudil and bimatoprost/ timolol in the collected endpoints on the quality of life.

In the category of side effects, in addition to the negative effect in the endpoint of discontinuation due to AEs, there is also a negative effect in the endpoint of ocular AEs. However, the most common events are predominantly asymptomatic events that often do not affect patients. In the overall assessment of the available results, the negative effects in the endpoints of discontinuation due to AEs and ocular AEs are therefore insufficient to derive a minor benefit of latanoprost/ netarsudil.

In the overall assessment, an additional benefit of latanoprost/ netarsudil over the appropriate comparator therapy bimatoprost/ timolol for adults with primary open-angle glaucoma or ocular hypertension for whom monotherapy with a prostaglandin or netarsudil provides insufficient IOP reduction is not proven.

2.2 Number of patients or demarcation of patient groups eligible for treatment

Number of patients or demarcation of patient groups eligible for treatment

The information on the number of patients is based on the target population in statutory health insurance (SHI).

In the benefit assessment, patients who were pretreated with prostaglandin analogue monotherapy were identified as the relevant sub-population. The SHI target population derived by the pharmaceutical company corresponds to this relevant sub-population.

The number of patients in the SHI target population stated by the pharmaceutical company is subject to uncertainties due to the methodological procedure in the overall assessment.

2.3 Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Roclanda (active ingredient: latanoprost/ netarsudil) at the following publicly accessible link (last access: 7 June 2023):

https://www.ema.europa.eu/en/documents/product-information/roclanda-epar-product-information_en.pdf

Treatment with latanoprost/ netarsudil should only be initiated and monitored by doctors experienced in the treatment of elevated intraocular pressure in the case of open-angle glaucoma or ocular hypertension.

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 15 May 2023).

The treatment duration is assumed to be one year (365 days), even if the actual treatment duration varies from patient to patient and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

In the product information for the beta-blockers timolol, betaxolol and levobunolol, which are part of the appropriate comparator therapy for the free combination with prostaglandin analogues or prostamides, the dosage can be reduced from 1 drop twice daily to 1 drop once daily if the intraocular pressure is adjusted to the desired value during regular monitoring.

For each active ingredient and each fixed combination, the most favourable medicinal product is used, regardless of whether it contains preservatives or not.

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Latanoprost | netarsudil	continuously, 1 x day	365	1	365.0
Appropriate comparator therapy				
Fixed combination of beta-blockers and prostaglandin analogues or prostamide				
Bimatoprost | timolol	continuously, 1 x day	365	1	365.0
Latanoprost | timolol				
Travoprost | Timolol				
Free combination of beta-blockers and prostaglandin analogues or prostamide				
Bimatoprost	continuously, 1 x day	365	1	365.0
Latanoprost				
Travoprost				
Tafluprost				
Timolol	Continuously, 2 x daily	365	1	365.0
Levobunolol				
Betaxolol				

Consumption:

For consumption, standardised 0.05 ml per drop, corresponding to the data of the official version of the ATC index with DDD information for Germany in 2023, is used. The treatment of both eyes is shown[3]

The shelf life after opening the packaging was taken into account in the treatment cost calculation.

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Latanoprost | netarsudil	0.1 ml	0.1 ml	1 x 0.1 ml	365.0	365 x 0.1 ml
Appropriate comparator therapy					
Fixed combination of beta-blockers and prostaglandin analogues or prostamide					
Bimatoprost | timolol	0.1 ml	0.1 ml	1 x 0.1 ml	365.0	365 x 0.1 ml
Latanoprost | timolol	0.1 ml	0.1 ml	1 x 0.1 ml	365.0	365 x 0.1 ml
Travoprost | timolol	0.1 ml	0.1 ml	1 x 0.1 ml	365.0	365 x 0.1 ml
Free combination of beta-blockers and prostaglandin analogues or prostamide					
Bimatoprost	0.1 ml	0.1 ml	1 x 0.1 ml	365.0	365 x 0.1 ml
Latanoprost	0.1 ml	0.1 ml	1 x 0.1 ml	365.0	365 x 0.1 ml
Travoprost	0.1 ml	0.1 ml	1 x 0.1 ml	365.0	365 x 0.1 ml
Tafluprost	0.1 ml	0.1 ml	1 x 0.1 ml	365.0	365 x 0.1 ml
timolol	0.1 ml	0.2 ml	2 x 0.1 ml	365.0	730 x 0.1 ml
Levobunolol	0.1 ml	0.2 ml	2 x 0.1 ml	365.0	730 x 0.1 ml
Betaxolol	0.1 ml	0.2 ml	2 x 0.1 ml	365.0	730 x 0.1 ml

[3] https://www.bfarm.de/SharedDocs/Downloads/DE/Kodiersysteme/ATC/atc-ddd-amtlich-2023.pdf?__blob=publicationFile [last accessed on: 6 June 2023

Costs:

Costs of the medicinal products:

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Latanoprost 0.05 mg | Netarsudil 0.28 mg	3 x 2.5 ml Egtts	€ 85.17	€ 2.00	€ 7.01	€ 76.16
Appropriate comparator therapy					
Bimatoprost 0.3 mg | Timolol 6.83 mg[4]	3 x 3 ml Egtts	€ 52.60	€ 2.00	€ 3.27	€ 47.33
Latanoprost 0.05 mg | Timolol 6.83 mg[4]	6 x 2.5 ml Egtts	€ 74.86	€ 2.00	€ 5.03	€ 67.83
Travoprost 0.04 mg | Timolol 6.83 mg[4]	6 x 2.5 ml Egtts	€ 74.86	€ 2.00	€ 5.03	€ 67.83
Levobunolol 2 mg[4]	90 x 0.4 ml Egtts	€ 25.50	€ 2.00	€ 0.00	€ 23.50
Bimatoprost 0.1 mg[4]	3 x 3 ml Egtts	€ 32.74	€ 2.00	€ 1.70	€ 29.04
Latanoprost 0.05 mg[4]	6 x 2.5 ml Egtts	€ 52.16	€ 2.00	€ 3.23	€ 46.93
Travoprost 0.04 mg[4]	6 x 2.5 ml Egtts	€ 52.16	€ 2.00	€ 3.23	€ 46.93
Tafluprost 15 µg[4]	3 x 2.5 ml Egtts	€ 33.87	€ 2.00	€ 1.79	€ 30.08
Timolol 3.42 mg[4]	6 x 2.5 ml Egtts	€ 17.09	€ 2.00	€ 0.46	€ 14.63
Betaxolol 5.59 mg[4]	3 x 5 ml Egtts	€ 18.55	€ 2.00	€ 0.00	€ 16.55
Abbreviations: Egtts = eye drops					

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Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

[4] Fixed reimbursement rate

Because there are no regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, no costs for additionally required SHI services had to be taken into account.

2.5 Medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with latanoprost/ netarsudil

According to Section 35a, paragraph 3, sentence 4, the G-BA designates all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

In accordance with Section 2, paragraph 1, sentence 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), only medicinal products containing active ingredients whose effects are not generally known in medical science at the time of initial marketing authorisation are to be considered within the framework of the designation of medicinal products with new active ingredients that can be used in a combination therapy. According to Section 2, paragraph 1, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), a medicinal product with a new active ingredient is considered to be a medicinal product with a new active ingredient for as long as there is dossier protection for the medicinal product with the active ingredient that was authorised for the first time.

The designation of the combination therapies is based solely on the specifications according to Section 35a, paragraph 3, sentence 4. The G-BA does not conduct a substantive review based on the generally recognised state of medical knowledge. Thus, the designation is not associated with a statement as to the extent to which a therapy with the designated medicinal product with new active ingredient in combination with the medicinal product to be assessed corresponds to the generally recognised state of medical knowledge.

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

At its session on 6 July 2021, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 9 December 2022, the pharmaceutical company submitted a dossier for the benefit assessment of latanoprost/ netarsudil to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 15 December 2022 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the combination of active ingredients latanoprost/ netarsudil.

The dossier assessment by the IQWiG was submitted to the G-BA on 13 March 2023, and the written statement procedure was initiated with publication on the G-BA website on 15 March 2023. The deadline for submitting statements was 5 April 2023.

The oral hearing was held on 2 May 2023.

By letter dated 3 May 2023, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by IQWiG was submitted to the G-BA on 26 May 2023.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing was discussed at the session of the subcommittee on 6 June 2023, and the proposed resolution was approved.

At its session on 15 June 2023, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	6 July 2021	Determination of the appropriate comparator therapy
Working group Section 35a	26 April 2023	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	2 May 2023; 3 May 2023	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	10.05.2023; 31.05.2023	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Subcommittee Medicinal products	6 June 2023	Concluding discussion of the draft resolution
Plenum	15 June 2023	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 15 June 2023

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The Chair

Prof. Hecken