Resolution

of the Federal Joint Committee 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

At its session on 15 June 2023, the Federal Joint Committee (G-BA) resolved to amend the Pharmaceuticals Directive (AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended by the publication of the resolution of D Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

I. Annex XII shall be amended in alphabetical order to include the active ingredient Latanoprost/Netarsudil as follows:

Latanoprost/Netarsudil

Resolution of: 15 June 2023
Entry into force on: 15 June 2023
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 7 January 2023):

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 June 2023):

See therapeutic indication according to marketing authorisation.

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

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

Extent and likelihood of additional benefit of latanoprost/ netarsudil over bimatoprost/ timolol:

An additional benefit is not proven.

Study results according to endpoints:[1]

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

[1] Data from the dossier assessment of the IQWiG (A22-129) and from the addendum (A23-39), unless otherwise indicated.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No relevant difference for the benefit assessment
Morbidity	↔	No relevant difference for the benefit assessment
Health-related quality of life	↔	No relevant difference for the benefit assessment
Side effects	↓	negative effect in the endpoints discontinuation due to AEs and in detail ocular AEs
Explanations: ↑: statistically significant and relevant positive effect with low/unclear reliability of data ↓: statistically significant and relevant negative effect with low/unclear reliability of data ↑↑: statistically significant and relevant positive effect with high reliability of data ↓↓: statistically significant and relevant negative effect with high reliability of data ↔: no statistically significant or relevant difference ∅: There are no usable data for the benefit assessment. n.a.: not assessable		

MERCURY 3 study: latanoprost/netarsudil vs bimatoprost/ timolol

Study design: randomised, double-blind, parallel-group study

Relevant sub-population: Pretreatment with prostaglandin monotherapy

Mortality

MERCURY 3 study Endpoint	latanoprost/netarsudil		bimatoprost/timolol		latanoprost/ netarsudil vs bimatoprost/ timolol
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[a]
Overall survival					
	116	0 (0)	95	0 (0)	–

Morbidity

MERCURY 3 study Endpoint	latanoprost/netarsudil		bimatoprost/ timolol		latanoprost/ netarsudil vs bimatoprost/ timolol
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[a]
Best corrected visual acuity[f]					
Improvement ≥ 0.2 logMAR units	110	2 (2)	95	3 (3)	0.6 [0.1; 3.4]; 0.618[a]
Deterioration ≥ 0.2 logMAR units	110	2 (2)	95	2 (2)	0.9 [0.1; 6.0]; 0.952[a]
Improvement ≥ 0.3 logMAR units	110	0 (0)	95	1 (1)	0.3 [0.0; 7.0]; 0.358[a]
Deterioration ≥ 0.3 logMAR units	110	0 (0)	95	1 (1)	0.3 [0.0; 7.0]; 0.358[a]
NEI VFQ-25[b] – General health status subscale					
Improvement	89	16 (18)	88	14 (16)	1.1 [0.6; 2.2]; 0.793
Deterioration	89	17 (19)	88	13 (15)	1.3 [0.7; 2.5]; 0.532

Health-related quality of life

MERCURY 3 study Endpoint	Latanoprost/ netarsudil		Bimatoprost/ timolol		Latanoprost/ netarsudil vs bimatoprost/ timolol
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[a]
NEI VFQ-25[b] sum score[h]					
Improvement	86	2 (2)	88	2 (2)	1.0 [0.1; 7.1]; > 0.999
Deterioration	86	2 (2)	88	2 (2)	1.0 [0.1; 7.1]; > 0.999

MERCURY 3 study Endpoint	Latanoprost/ netarsudil		Bimatoprost/ timolol		Latanoprost/ netarsudil vs bimatoprost/ timolol
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[a]
SF-36 – Physical Component Summary (PCS) score[c]					
Improvement	86	5 (6)	88	4 (5)	1.3 [0.4; 4.6]; 0.773
Deterioration	86	1 (1)	88	5 (6)	0.2 [0.0; 1.7]; 0.124
SF-36 – Mental Component Summary (MCS) score[d]					
Improvement	86	9 (10)	88	7 (8)	1.3 [0.5; 3.4]; 0.600
Deterioration	86	5 (6)	88	7 (8)	0.7 [0.2; 2.2]; 0.682

Side effects

MERCURY 3 study Endpoint	Latanoprost/ netarsudil		Bimatoprost/ timolol		Latanoprost/ netarsudil vs bimatoprost/ timolol
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[a]
Adverse events[g] *(presented additionally)*					
	116	93 (80)	95	58 (61)	–
Serious adverse events (SAE)					
	116	5 (4)	95	1 (1)	4.1 [0.5; 34.5]; 0.184
Discontinuation due to AEs					
	116	18 (16)	95	1 (1)	14.7 [2.0; 108.4]; < 0.001
Ocular AEs[e]					
	116	75 (65)	95	35 (37)	1.8 [1.3; 2.4]; < 0.001
Ocular SAEs					
	116	0 (0)	95	0 (0)	–

MERCURY 3 study Endpoint	Latanoprost/ netarsudil		Bimatoprost/ timolol		Latanoprost/ netarsudil vs bimatoprost/ timolol
	N	Patients with event n (%)	N	Patients with event n (%)	Effect estimator [95% CI] p value[a]

a. Own calculation, unconditional exact test (CSZ method according to Martín Andrés A & Silva Mato A.).
b. Percentage of patients with an increase (improvement) and decrease (deterioration) in score by ≥ 15.15 points at month 6 compared to the start of the study.
c. Percentage of patients with an increase (improvement) or decrease (deterioration) in the PCS score by ≥ 9.4 points (corresponds to 15% of the scale range) at month 6 compared to the start of the study; no data are available for the subscales of the SF-36.
d. Percentage of patients with an increase (improvement) or decrease (deterioration) of the MCS score by ≥ 9.6 points (corresponds to 15% of the scale range) at month 6 compared to the start of the study; no data available for the subscales of the SF-36.
e. The most frequently occurring events (in each case in the intervention vs comparator arm) are: Conjunctival hyperaemia (PT) (30% vs 15%), conjunctival haemorrhage (PT) (12% vs 3%) and cornea verticillata (PT) (11% vs 0)
f. refers to both eyes; percentage of patients with an increase or decrease in visual acuity of ≥ 0.2 logMAR units, corresponding to ≥ 10 EDTRS letters (or ≥ 0.3 logMAR units, corresponding to ≥ 15 EDTRS letters) compared to the start of the study at month 6. One line with 5 letters corresponds to 0.1 logMAR (scale range from -0.3 logMAR to 1.0 logMAR). Lower (decreasing) or higher (increasing) values on the logMAR scale mean an improvement or deterioration of the symptomatology.
g. Potentially includes events of the underlying disease; in the present data basis, it is assumed that the disease-related events included in these evaluations do not have any relevant impact on the study results, especially on the magnitude.
h. The following subscales were recorded: General vision, eye pain, near vision, distance vision, social functioning, psychological well-being, performance of social roles, dependence on others, problems with driving a car, problems with colour vision, peripheral vision. There are no statistically significant differences.

Abbreviations used:
ETDRS = Early Treatment Diabetic Retinopathy Study; CI = confidence interval; logMAR = logarithm of the minimum angle of resolution; MCS = Mental Component Summary; n: Number of patients with (at least 1) event; N = number of patients evaluated; n.r. = not reached; NEI VFQ-25: National Eye Institute Function Questionnaire-25; PCS = Physical Component Summary; PT = preferred term; RCT = randomised controlled trial; RR = relative risk; SOC = system organ class; SAE = serious adverse event; AE = adverse event; vs = versus

2. Number of patients or demarcation of patient groups eligible for treatment

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

approx. 87,800 patients

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.

4. Treatment costs

Annual treatment costs:

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

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Latanoprost + netarsudil	€ 370.65
Appropriate comparator therapy:	
Combination therapy of beta-blocker + prostaglandin analogue or prostamide as free or fixed combination	€ 149.80 - € 337.00[2]

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 May 2023)

Costs for additionally required SHI services: not applicable

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

Medicinal products with new active ingredients pursuant to Section 35a, paragraph 3 sentence 4 SGB V are medicinal products with the following new active ingredients which, on the basis of the marketing authorisation under Medicinal Products Act, can be used in a combination therapy with latanoprost/ netarsudil 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:

[2] The range is made up of the less expensive combination therapy “timolol + latanoprost or travoprost” and a more costly combination therapy “levobunolol + tafluprost”.

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

A designation of the concomitant active ingredients shall be made in a further resolution. The adoption of the resolution will be preceded by a written and oral written statement procedure pursuant to Chapter 5, Section 19 of the Regulation, in the course of which the pharmaceutical companies concerned will be given the opportunity to comment on the planned designation.

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 15 June 2023.

The justification to this resolution will be published on the website of the G-BA at www.g-ba.de.

Berlin, 15 June 2023

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

Prof. Hecken