Gemeinsamer Bundesausschuss

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) and Annex XIIa – Combinations of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Alirocumab (new therapeutic indication: hypercholesterolaemia, ≥ 8 years to 17 years)

of 6 June 2024

At its session on 6 June 2024, 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. In Annex XII, the following information shall be added after No. 4 to the information on the benefit assessment of Alirocumab in accordance with the resolution of 2 May 2019:

Alirocumab

Resolution of: 6 June 2024
Entry into force on: 6 June 2024
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 15 November 2023):

Primary hypercholesterolaemia and mixed dyslipidaemia

Praluent is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, and in paediatric patients 8 years of age and older with heterozygous familial hypercholesterolaemia (HeFH) as an adjunct to diet:

- in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin or,
- alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

Therapeutic indication of the resolution (resolution of 6 June 2024):

Praluent is indicated in paediatric patients 8 to 17 years of age with heterozygous familial hypercholesterolaemia (HeFH) as an adjunct to diet:

- in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin or,
- alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

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

a) <u>Paediatric patients 8 to 17 years of age with heterozygous familial hypercholesterolaemia in whom dietary and medicinal treatment options for lipid lowering have not been exhausted</u>

Appropriate comparator therapy for alirocumab:

- Maximum tolerated medicinal therapy according to the doctor's instructions, taking into account statins, cholesterol absorption inhibitors and anion exchangers

Extent and probability of the additional benefit of alirocumab compared to the appropriate comparator therapy:

An additional benefit is not proven.

b) Paediatric patients 8 to 17 years of age with heterozygous familial hypercholesterolaemia in whom dietary and medicinal treatment options for lipid lowering have been exhausted

Appropriate comparator therapy for alirocumab:

- Evolocumab (10 years and older) or LDL apheresis (as an "ultima ratio" for therapy-refractory courses), if necessary with concomitant lipid-lowering medicinal therapy

Extent and probability of the additional benefit of alirocumab compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Paediatric patients 8 to 17 years of age with heterozygous familial hypercholesterolaemia in whom dietary and medicinal treatment options for lipid lowering have not been exhausted

There are no assessable data.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	There are no assessable data.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	∅	No data available.
Side effects	n.a.	There are no assessable data.

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
∅: No data available
n.a.: not assessable

1 Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A23-136) unless otherwise indicated.

b) Paediatric patients 8 to 17 years of age with heterozygous familial hypercholesterolaemia in whom dietary and medicinal treatment options for lipid lowering have been exhausted

There are no assessable data.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	There are no assessable data.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	∅	No data available.
Side effects	n.a.	There are no assessable data.

Explanations:
↑: statistically significant and relevant positive effect with low/unclear reliability of data
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↑↑: 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
∅: No data available.
n.a.: not assessable

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

a) Paediatric patients 8 to 17 years of age with heterozygous familial hypercholesterolaemia in whom dietary and medicinal treatment options for lipid lowering have not been exhausted

Approx. 950 - 1,170 patients

b) Paediatric patients 8 to 17 years of age with heterozygous familial hypercholesterolaemia in whom dietary and medicinal treatment options for lipid lowering have been exhausted

Approx. 8 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 Praluent (active ingredient: alirocumab) at the following publicly accessible link (last access: 15 March 2024):

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

The prescription restrictions for alirocumab in the Pharmaceuticals Directive Annex III must be taken into account.

4. Treatment costs

Annual treatment costs:

a) Paediatric patients **8 to 17 years** of age with heterozygous familial hypercholesterolaemia in whom dietary and medicinal treatment options for lipid lowering have not been exhausted

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Alirocumab as monotherapy	€ 2,825.05 - € 5,671.83
Pravastatin[2]	€ 45.63 - € 68.95
Cholestyramine	€ 87.69 - € 1,322.10
Ezetimibe	€ 96.14
Alirocumab in combination with other lipid-lowering therapies (including statin)	
Alirocumab + pravastatin	€ 2,870.68 - € 5,740.78
Alirocumab + pravastatin[2] + ezetimibe	€ 2,966.82 - € 5,836.92
Alirocumab + pravastatin[2] + cholestyramine	€ 2,958.37 - € 7,062.89
Alirocumab + pravastatin[2] + cholestyramine + ezetimibe	€ 3,054.51 - € 7,159.03
Alirocumab in combination with other lipid-lowering therapies (except statin)	
Alirocumab + ezetimibe	€ 2,921.19 - € 5,767.98
Alirocumab + cholestyramine	€ 2,912.74 - € 6,993.94
Alirocumab + cholestyramine + ezetimibe	€ 3,008.88 - € 7,090.08
Appropriate comparator therapy:	
Monotherapy	
Pravastatin[2]	€ 45.63 - € 68.95
Cholestyramine	€ 87.69 - € 1,322.10
Ezetimibe	€ 96.14
Combination therapies	
Pravastatin[2] + ezetimibe	€ 141.77 - € 165.09
Pravastatin[2] + cholestyramine	€ 133.32 - € 1,391.05
Pravastatin[2] + cholestyramine + ezetimibe	€ 229.46 - € 1,487.19
Ezetimibe + cholestyramine	€ 183.83 - € 1,418.24

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 May 2024

2 Pravastatin is shown as example for the statin group.

b) Paediatric patients **8 to 17 years** of age with heterozygous familial hypercholesterolaemia in whom dietary and medicinal treatment options for lipid lowering have been exhausted

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Alirocumab as monotherapy	€ 2,825.05 - € 5,671.83
Pravastatin[2]	€ 45.63 - € 68.95
Cholestyramine	€ 87.69 - € 1,322.10
Ezetimibe	€ 96.14
LDL apheresis	€ 23,150.18 - € 67,522.12
Alirocumab + LDL apheresis	€ 25,975.23 - € 73,193.95
Alirocumab in combination with other lipid-lowering therapies (including statin) including LDL apheresis	
Alirocumab + pravastatin[2] + LDL apheresis	€ 26,020.86 - € 73,262.90
Alirocumab + pravastatin[2] + cholestyramine + LDL apheresis	€ 26,108.55 - € 74,585.00
Alirocumab + pravastatin[2] + ezetimibe + LDL apheresis	€ 26,117.00 - € 73,359.04
Alirocumab + pravastatin[2] + ezetimibe + cholestyramine + LDL apheresis	€ 26,204.69 - € 74,681.15
Alirocumab in combination with other lipid-lowering therapies (excluding statin) including LDL apheresis	
Alirocumab + ezetimibe + LDL apheresis	€ 26,071.37 - € 73,290.10
Alirocumab + cholestyramine + LDL apheresis	€ 26,062.92 - € 74,516.06
Alirocumab + ezetimibe + cholestyramine + LDL-apheresis	€ 26,159.06 - € 74,612.20
Appropriate comparator therapy:	
Evolocumab (10 years and older) or LDL apheresis (as an "ultima ratio" for therapy-refractory courses), if necessary with concomitant lipid-lowering medicinal therapy	
Evolocumab as monotherapy	€ 5,360.07 - € 5,781.14
LDL apheresis as monotherapy	€ 23,150.18 - € 67,522.12
Pravastatin[2]	€ 45.63 - € 68.95
Cholestyramine	€ 87.69 - € 1,322.10[3]
Ezetimibe	€ 96.14
Evolocumab if necessary + concomitant lipid-lowering medicinal therapy (including statin)	
Evolocumab if necessary + pravastatin[2]	€ 5,405.70 - € 5,850.09
Evolocumab if necessary + pravastatin[2] + ezetimibe	€ 5,501.84 - € 5,946.23
Evolocumab if necessary + pravastatin[2]+ cholestyramine	€ 5,537.24 - 7,172.19
Evolocumab if necessary + pravastatin[2] + ezetimibe + cholestyramine	€ 5,633.38 - € 7,268.34
Evolocumab if necessary + concomitant lipid-lowering medicinal therapy (except statin)	

3 The lower limit for 10-year-old children is €131.54 and is within the range shown.

Evolocumab if necessary + ezetimibe	€ 5,456.21 - € 5,877.28
Evolocumab if necessary + cholestyramine	€ 5,491.61 - € 7,103.25
Evolocumab if necessary + ezetimibe + cholestyramine	€ 5,587.75 - € 7,199.39
LDL apheresis if necessary + concomitant lipid-lowering medicinal therapy (including statin)	
LDL apheresis if necessary + pravastatin[2]	€ 23,195.81 - € 67,591.07
LDL apheresis if necessary + pravastatin[2] + ezetimibe	€ 23,291.95 - € 67,687.21
LDL apheresis if necessary + pravastatin[2]+ cholestyramine	€ 23,283.50 - € 68,913.17
LDL apheresis if necessary + pravastatin[2] + ezetimibe + cholestyramine	€ 23,379.64 - € 69,009.31
LDL apheresis if necessary + concomitant lipid-lowering medicinal therapy (except statin)	
LDL apheresis if necessary + ezetimibe	€ 23,246.32 - € 67,618.26
LDL apheresis if necessary + cholestyramine	€ 23,237.87 - € 68,844.22
LDL apheresis if necessary + ezetimibe + cholestyramine	€ 23,334.01 - € 68,940.37

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 May 2024

Costs for additionally required SHI services: not applicable

5. Designation of 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 the assessed medicinal product

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

a) Paediatric patients 8 to 17 years of age with heterozygous familial hypercholesterolaemia in whom dietary and medicinal treatment options for lipid lowering have not been exhausted

The following medicinal products with new active ingredients that can be used in a combination therapy with alirocumab in the therapeutic indication of the resolution on the basis of the marketing authorisation under Medicinal Products Act are named (active ingredients and invented names) in accordance with Section 35a, paragraph 3, sentence 4 SGB V:

evolocumab (Repatha) [10 years and older]

b) Paediatric patients 8 to 17 years of age with heterozygous familial hypercholesterolaemia in whom dietary and medicinal treatment options for lipid lowering have been exhausted

The following medicinal products with new active ingredients that can be used in a combination therapy with alirocumab in the therapeutic indication of the resolution on the basis of the marketing authorisation under Medicinal Products Act are named (active ingredients and invented names) in accordance with Section 35a, paragraph 3, sentence 4 SGB V:

evolocumab (Repatha) [10 years and older]

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. **In Annex XIIa of the Pharmaceuticals Directive, the following information shall be added in alphabetical order:**

"Active ingredient of the assessed medicinal product

Alirocumab

Resolution according to Section 35a paragraph 3 SGB V from

6 June 2024

Therapeutic indication of the resolution

Praluent is indicated in paediatric patients 8 to 17 years of age with heterozygous familial hypercholesterolaemia (HeFH) as an adjunct to diet:

- in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin or,
- alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

Patient group a

Paediatric patients aged 8 to 17 years with heterozygous familial hypercholesterolaemia in whom dietary and medicinal treatment options for lipid lowering have not been exhausted

Naming of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V (active ingredients and invented names[2])

evolocumab (Repatha) [10 years and older]

Period of validity of the designation (since... or from... to)

Since 6 June 2024

Patient group b

Paediatric patients aged 8 to 17 years with heterozygous familial hypercholesterolaemia in whom dietary and medicinal treatment options for lipid lowering have been exhausted

Naming of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V (active ingredients and invented names[2])

evolocumab (Repatha) [10 years and older]

Period of validity of the designation (since... or from... to)

Since 6 June 2024

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.

III. The resolution will enter into force on the day of its publication on the website of the G-BA on 6 June 2024.

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

Berlin, 6 June 2024

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

Prof. Hecken