Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee on an Amendment of the Pharmaceuticals Directive (AM-RL)
Annex XII –Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Inclisiran (Primary hypercholesterolaemia or mixed dyslipidaemia)

of 15 July 2021

At its session on 15 July 2021, 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 on DD. 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 inclisiran as follows:

Inclisiran

Resolution of: 15 July 2021
Entry into force on: 15 July 2021
BAnz AT TT. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 9 December 2020):

Leqvio is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, 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 statin dose 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 15 July 2021):

see therapeutic indication according to marketing authorisation.

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

a) Adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia who have not yet exhausted medicinal and dietary options to reduce lipid levels

Appropriate comparator therapy:

- 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 inclisiran compared to the appropriate comparator therapy:

An additional benefit is not proven.

b) Adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia who have already exhausted medicinal (except evolocumab or alirocumab) and dietary optionsto reduce lipid levels

Appropriate comparator therapy:

- Evolocumab[1] or alirocumab or LDL apheresis (as an "ultima ratio" for therapy-refractory courses), if necessary with concomitant medicinal-based lipid-lowering therapy.

[1] The requirements regarding the prescription restriction of the Pharmaceutical Directive (AM-RL) Annex III must be observed.

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

An additional benefit is not proven.

Study results according to endpoints:[2]

a) Adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia who have not yet exhausted medicinal and dietary options to reduce lipid levels

There are no usable data for the benefit assessment.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	No data on benefit assessment are available.
Morbidity	∅	No data on benefit assessment are available.
Health-related quality of life	∅	No data on benefit assessment are available.
Side effects	∅	No data on benefit assessment are available.
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 calculable		

b) Adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia who have already exhausted medicinal (except evolocumab or alirocumab) and dietary optionsto reduce lipid levels

There are no usable data for the benefit assessment.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	No data on benefit assessment are available.
Morbidity	∅	No data on benefit assessment are available.
Health-related quality of life	∅	No data on benefit assessment are available.
Side effects	∅	No data on benefit assessment are available.
Explanations:		

[2] Data from the dossier assessment of the IQWiG (A21-13) unless otherwise indicated.

↑	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	

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

a) Adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia who have not yet exhausted medicinal and dietary options to reduce lipid levels

approx. 271,750 to 389,900 patients

b) Adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia who have already exhausted medicinal (except evolocumab or alirocumab) and dietary optionsto reduce lipid levels

approx. 13,000 – 21,000 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 Leqvio (active ingredient: inclisiran) at the following publicly accessible link (last access: 8 June 2021):

https://www.ema.europa.eu/documents/product-information/leqvio-epar-product-information_de.pdf

The prescription restrictions for lipid-lowering agents in accordance with the Pharmaceutical Directive Annex III No. 35 must be taken into account.

4. Treatment costs

Annual treatment costs:

a) Adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia who have not yet exhausted medicinal and dietary options to reduce lipid levels

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Inclisiran as monotherapy	€ 5,464.42
Simvastatin[3]	€ 68.77 - € 98.19
Colesevelam	€ 2,346.22
Cholestyramine	€ 1,051.42
Ezetimibe	€ 149.43
Inclisiran in combination with other lipid-lowering therapies (including statin)	
Inclisiran + simvastatin[3]	€ 5,533.19 - € 5,562.61
Inclisiran+ simvastatin [3] + ezetimibe	€ 5,682.62 - € 5,712.04
Inclisiran + simvastatin [3] + colesevelam	€ 7,879.41 - € 7,908.83
Inclisiran + simvastatin [3] + cholestyramine	€ 6,584.61 - € 6,614.02
Inclisiran + simvastatin, [3] + colesevelam + ezetimibe	€ 8,028.84 - € 8,058.26
Inclisiran + simvastatin[3,] + cholestyramine + ezetimibe	€ 6,734.04 - € 6,763.46
Inclisiran in combination with other lipid-lowering therapies (except statin)	
Inclisiran + ezetimibe	€ 5,613.85
Inclisiran + colesevelam	€ 7,810.64
Inclisiran + cholestyramine	€ 6,515.84
Inclisiran + colesevelam + ezetimibe	€ 7,960.07
Inclisiran + cholestyramine + ezetimibe	€ 6,665.27
Appropriate comparator therapy:	
Monotherapies	
Simvastatin	€ 68.77 - € 98.19
Colesevelam	€ 2,346.22
Cholestyramine	€ 1,051.42
Ezetimibe	€ 149.43
Combination therapy	
Simvastatin[3,] + ezetimibe	€ 218.20 - € 247.62
Simvastatin, [3] + colesevelam	€ 2,414.99 - € 2,444.41
Simvastatin[3,] + cholestyramine	€ 1,120.19 - € 1,149.60
Simvastatin[3,] + colesevelam + ezetimibe	€ 2,564.42 - € 2,593.84
Simvastatin, [3] + cholestyramine + ezetimibe	€ 1,269.62 - € 1,299.04

[3] Simvastatin is shown as example for the statin group Simvastatin is presented in the daily dosage range of 40 mg to 80 mg

Designation of the therapy	Annual treatment costs/patient
Ezetimibe + colesevelam	€ 2,495.65
Ezetimibe + cholestyramine	€ 1,200.85

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 June 2021)

b) Adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia who have already exhausted medicinal (except evolocumab or alirocumab) and dietary optionsto reduce lipid levels

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Inclisiran as monotherapy	€ 5,464.42
Simvastatin	€ 68.77 - € 98.19
Colesevelam	€ 2,346.22
Cholestyramine	€ 1,051.42
Ezetimibe	€ 149.43
LDL apheresis	€ 23,118.86 - € 67,459.60
Inclisiran + LDL apheresis	€ 28,583.28 - € 72,924.02
Inclisiran in combination with other lipid-lowering therapies (excluding statin) including LDL apheresis	
Inclisiran + simvastatin[3,] + LDL apheresis	€ 28,652.05 - € 73,022.21
Inclisiran + simvastatin[3,] + ezetimibe + LDL apheresis	€ 28,801.48 - € 73,171.64
Inclisiran + simvastatin[3,] + colesevelam + LDL apheresis	€ 30,998.27 - € 75,368.43
Inclisiran + simvastatin[3,] + cholestyramine + LDL apheresis	€ 29,703.47 - € 74,073.62
Inclisiran + simvastatin[3,] + ezetimibe + colesevelam + LDL apheresis	€ 31,147.70 - € 75,517.86
Inclisiran + Simvastatin[3,] + ezetimibe + cholestyramine + LDL apheresis	€ 29,852.90 - € 74,223.06
Inclisiran in combination with other lipid-lowering therapies (excluding statin) including LDL apheresis	
Inclisiran + ezetimibe + LDL apheresis	€ 28,732.71 - € 73,073.45
Inclisiran + colesevelam + LDL apheresis	€ 30,929.50 - € 75,270.24
Inclisiran + cholestyramine + LDL apheresis	€ 29,634.70 - € 73,975.44
Inclisiran + ezetimibe + colesevelam + LDL apheresis	€ 31,078.93 - € 76,419.67
Inclisiran + ezetimibe + cholestyramine + LDL apheresis	€ 29,784.13 - € 74,124.87
Appropriate comparator therapy:	

Evolocumab or LDL apheresis (as an "ultima ratio" for therapy-refractory courses), if necessary with concomitant medicinal-based lipid-lowering therapy.	
Evolocumab as monotherapy	€ 5,885.99 - € 6,345.47
Alirocumab as monotherapy	€ 6,228.59 - € 6,715.24
LDL apheresis	€ 23,118.86 - € 67,459.60
Evolocumab if necessary + accompanying medication-based lipid-lowering therapy (including statin)	
Evolocumab if applicable + simvastatin [3]	€ 5,954.75 - € 6,443.66
Evolocumab if applicable + simvastatin[3] + ezetimibe	€ 6,104.18 - € 6,593.09
Evolocumab if applicable + simvastatin[3] + colesevelam	€ 8,300.97 - € 8,789.88
Evolocumab if applicable + simvastatin[3] + cholestyramine	€ 7,006.17 - € 7,495.08
Evolocumab if applicable + simvastatin[3] + ezetimibe + colesevelam	€ 8,450.40 - € 8,939.31
Evolocumab if applicable + simvastatin[3] + ezetimibe + cholestyramine	€ 7,155.60 - € 7,644.51
Evolocumab if necessary + accompanying medication-based lipid-lowering therapy (except statin)	
Evolocumab if applicable + ezetimibe	€ 6,035.42 - € 6,494.90
Evolocumab if applicable + colesevelam	€ 8,232.21 - € 8,691.69
Evolocumab if applicable + cholestyramine	€ 6,937.40 - € 7,396.89
Evolocumab if applicable + ezetimibe + colesevelam	€ 8,381.64 - € 8,841.12
Evolocumab if applicable + ezetimibe + cholestyramine	€ 7,086.84 - € 7,546.32
Alirocumab if necessary + accompanying medication-based lipid-lowering therapy (including statin)	
Alirocumab if applicable + simvastatin [3]	€ 6,297.36 - € 6,813.42
Alirocumab if applicable + simvastatin[3] + ezetimibe	€ 6,446.79 - € 6,962.85
Alirocumab if applicable + simvastatin[3] + colesevelam	€ 8,643.58 - € 9,159.64
Alirocumab if applicable + simvastatin[3] + cholestyramine	€ 7,348.78 - € 7,864.84
Alirocumab if applicable + simvastatin[3] + ezetimibe + colesevelam	€ 8,793.01 - € 9,309.07
Alirocumab if applicable + simvastatin[3] + ezetimibe + cholestyramine	€ 7,498.21 - € 8,014.27
Alirocumab if necessary + accompanying medication-based lipid-lowering therapy (except statin)	
Alirocumab if applicable + ezetimibe	€ 6,378.02 - € 12,329.09
Alirocumab if applicable + colesevelam	€ 8,574.81 - € 9,061.46

Alirocumab if applicable + cholestyramine	€ 7,280.01 - €7,766.66
Alirocumab if applicable + ezetimibe + colesevelam	€ 8,724.24 - € 9,210.89
Alirocumab if applicable + ezetimibe + cholestyramine	€ 7,429.44 - € 7,916.09
LDL apheresis if necessary + accompanying medication-based lipid-lowering therapy (including statin)	
LDL apheresis if necessary + simvastatin [3]	€ 23,187.63 - € 67,557.79
LDL apheresis if necessary + simvastatin[3] + ezetimibe	€ 23,337.06 - € 67,707.22
LDL apheresis if necessary + simvastatin[3] + colesevelam	€ 23,450.48 - € 69,904.01
LDL apheresis if necessary + simvastatin[3] + cholestyramine	€ 24,239.05 - € 68,609.20
LDL apheresis if necessary + simvastatin[3] + ezetimibe + colesevelam	€ 25,683.28 - € 70,053.44
LDL apheresis if necessary + simvastatin[3] + ezetimibe + cholestyramine	€ 24,388.48 - € 68,758.64
LDL apheresis if necessary + accompanying medication-based lipid-lowering therapy (except statin)	
LDL apheresis if necessary + ezetimibe	€ 23,268.29 - € 67,609.03
LDL apheresis if necessary + colesevelam	€ 25,465.08 - € 69,805.82
LDL apheresis if necessary + cholestyramine	€ 24,170.28 - € 68,511.02
LDL apheresis if necessary + ezetimibe + colesevelam	€ 25,614.51 - € 69,955.25
LDL apheresis if necessary + ezetimibe + cholestyramine	€24,319.71 - € 68,660.45

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 June 2021)

Costs for additionally required SHI services: not applicable

II. The resolution will enter into force on the day of its publication on the internet on the website of the G-BA on 15 July 2021.

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

Berlin, 15 July 2021

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

Prof. Hecken