Resolution

Gemeinsamer Bundesausschuss

of the Resolution of the Federal Joint Committee (G-BA) 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 Bempedoic acid/Ezetimibe (Primary hypercholesterolaemia or mixed dyslipidaemia)

of 15 April 2021

At its session on 15 April 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 combination of active ingredient bempedoic acid/ezetimibe as follows:

bempedoic acid/ezetimibe

Resolution of: 15 April 2021
Entry into force on: 15 April 2021
BAnz AT TT MM JJJJ Bx

Therapeutic indication (according to the marketing authorisation of 27 March 2020):

Nustendi is indicated in adults with primary hypercholesterolaemia (heterozygous familial and non-familial) or mixed dyslipidaemia, in addition to diet:

- in combination with a statin in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin in addition to ezetimibe,
- alone in patients who are either statin-intolerant or for whom a statin is contraindicated, and are unable to reach LDL-C goals with ezetimibe alone,
- in patients already being treated with the combination of bempedoic acid and ezetimibe as separate tablets with or without statin.

Therapeutic indication of the resolution (resolution from the 15 April 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 bempedoic acid/ezetimibe 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) and dietary options to reduce lipid levels

Appropriate comparator therapy:

– Evolocumab[1] 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 considered.

Extent and probability of the additional benefit of bempedoic acid/ezetimibe 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 relevant data in comparison with the appropriate comparator therapy that can be assessed.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	n.a.	No relevant data submitted.
Morbidity	n.a.	No relevant data submitted.
Health-related quality of life	n.a.	No relevant data submitted.
Side effects	n.a.	No relevant data submitted.
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		

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

There are no relevant data in comparison with the appropriate comparator therapy.

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.

[2] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A20-91) unless otherwise indicated.

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 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 patients

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

approx. 13 000 to 15 000 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 Nustendi (combination of active ingredients: bempedoic acid/ezetimibe) at the following publicly accessible link (last access: 12 March 2021):

https://www.ema.europa.eu/documents/product-information/nustendi-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:	
bempedoic acid/ezetimibe in monotherapy	€ 1,664.88
Simvastatin[3][4]	€ 52.78 – € 68.77
bempedoic acid/ezetimibe in combination with statin	Total
bempedoic acid/ezetimibe + simvastatin [3] [4]	€ 1,717.66 – € 1,733.65
Appropriate comparator therapy:	
Monotherapy	
Simvastatin [3] [5]	€ 68.77 – € 98.19
Colesevelam	€ 2,346.22
Cholestyramine	€ 1,051.42
Ezetimibe	€ 149.43
Combination therapy	Total:
Simvastatin[3, 5] + ezetimibe	€ 218.20 – € 247.62
Simvastatin[3, 5] + colesevelam	€ 2,414.99 – € 2,444.41
Simvastatin[3, 5] + cholestyramine	€ 1,120.19 – € 1,149.60
Simvastatin[3, 5] + colesevelam + ezetimibe	€ 2,564.42 – € 2,593.84
Simvastatin[3, 5] + cholestyramine + ezetimibe	€ 1,269.62 – € 1,299.03
Ezetimibe + colesevelam	€ 2,495.65
Ezetimibe + cholestyramine	€ 1,200.85

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

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

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
bempedoic acid/ezetimibe in monotherapy	€ 1,664.88

[3] Simvastatin is shown as example for the statin group
[4] Simvastatin is presented in the daily dose range of 20 mg to 40 mg, since, according to the product information for bempedoic acid, the combination therapy with simvastatin specifies a maximum dose of 40 mg simvastatin
[5] Simvastatin is presented in the daily dosage range of 40 mg to 80 mg

Simvastatin [3] [4]	€ 52.78 – € 68.77
LDL apheresis	€ 23,118.86 – € 67,459.60
bempedoic acid/ezetimibe + LDL apheresis	€ 24.783.74 - € 69.124,48
bempedoic acid/ezetimibe in combination with statin (including LDL apheresis)	Total
bempedoic acid/ezetimibe + simvastatin[3, 4] + LDL apheresis	€ 24,836.52 – € 69,193.25
Appropriate comparator therapy:	
Evolocumab as monotherapy	€ 5,885.985 - € 6,345.47
LDL apheresis	€ 23,118.86 – € 67,459.60
Evolocumab if applicable + accompanying medicinal lipid-lowering therapy (including statin)	Total:
Evolocumab if applicable + simvastatin[3, 5]	€ 5,954.75 – € 6,443.66
Evolocumab if applicable + simvastatin[3, 5] + ezetimibe	€ 6,104.18 – € 6,593.09
Evolocumab if applicable + simvastatin[3, 5] + colesevelam	€ 8,300.97 – € 8,789.88
Evolocumab if applicable + simvastatin[3, 5] + cholestyramine	€ 7,006.17 – € 7,495.08
Evolocumab if applicable + simvastatin[3, 5] + ezetimibe + colesevelam	€ 8,450.40 – € 8,939.31
Evolocumab if applicable + simvastatin[3, 5] + ezetimibe + cholestyramine	€ 7,155.60 – € 7,644.51
Evolocumab if applicable + Accompanying medicinal lipid-lowering therapy (except with statin)	Total:
Evolocumab if applicable + ezetimibe	€ 6,035.42 – € 6494.90
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
LDL apheresis if necessary + accompanying medication-based lipid-lowering therapy (including statin)	Total:
LDL apheresis if necessary + simvastatin[3, 5]	€ 23,187.63 – € 67,557.79
LDL apheresis if necessary + simvastatin[3, 5] + ezetimibe	€ 23,337.06 – € 67,707.22
LDL apheresis if necessary + simvastatin[3, 5] + colesevelam	€ 25,533.85 – € 69,904.01
LDL apheresis if necessary + simvastatin[3, 5] + cholestyramine	€ 24,239.05 – € 68,609.20
LDL apheresis if necessary + simvastatin[3, 5] + ezetimibe + colesevelam	€ 25,683.28 – € 70,053.44
LDL apheresis if necessary + simvastatin[3, 5]+ ezetimibe + cholestyramine	€ 24,388.48 – € 68,758.64

LDL apheresis if necessary + accompanying medication-based lipid-lowering therapy (except statin)	Total:
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 March 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 April 2021.

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

Berlin, 15 April 2021

Federal Joint Committee in accordance with Section 91 SGB V The chairman

Prof. Hecken