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
Setmelanotide (new therapeutic indication: obesity and control of hunger, POMC, PCSK1, LEPR deficiency or Bardet-Biedl syndrome, ≥ 2 to < 6 years)

of 21 August 2025

At their session on 21 August 2025, 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. 5 to the information on the benefit assessment of Setmelanotide in accordance with the resolution of 2 November 2023:

Setmelanotide

Resolution of: 21 August 2025
Entry into force on: 21 August 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 26 July 2024):

IMCIVREE is indicated for the treatment of obesity and the control of hunger associated with genetically confirmed Bardet-Biedl syndrome (BBS), loss-of-function biallelic pro-opiomelanocortin (POMC), including PCSK1, deficiency or biallelic leptin receptor (LEPR) deficiency in adults and children 2 years of age and above.

Therapeutic indication of the resolution (resolution of 21 August 2025):

IMCIVREE is indicated for the treatment of obesity and the control of hunger associated with genetically confirmed Bardet-Biedl syndrome (BBS), loss-of-function biallelic pro-opiomelanocortin (POMC), including PCSK1, deficiency or biallelic leptin receptor (LEPR) deficiency in children 2 to < 6 years of age.

1. Extent of the additional benefit and significance of the evidence

Setmelanotide is approved as a medicinal product for the treatment of rare diseases under Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999 on orphan drugs. In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional medical benefit is considered to be proven through the grant of the marketing authorisation.

The G-BA determines the extent of the additional benefit for the number of patients and patient groups for which there is a therapeutically significant additional benefit in accordance with Chapter 5 Section 12, paragraph 1, number 1, sentence 2 of its Rules of Procedure (VerfO) in conjunction with Section 5, paragraph 8 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), indicating the significance of the evidence. This quantification of the additional benefit is based on the criteria laid out in Chapter 5 Section 5, paragraph 7, numbers 1 to 4 of the Rules of Procedure (VerfO).

Children 2 to < 6 years of age with genetically confirmed Bardet-Biedl syndrome, POMC, PCSK1 or LEPR deficiency for the treatment of obesity and the control of hunger

Extent of the additional benefit and significance of the evidence of setmelanotide:

Hint for a non-quantifiable additional benefit since the scientific data does not allow quantification.

Study results according to endpoints:[1]

Children 2 to < 6 years of age with genetically confirmed Bardet-Biedl syndrome, POMC, PCSK1 or LEPR deficiency for the treatment of obesity and the control of hunger

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	↑	Advantage in BMI (z-score) at week 52 compared to baseline.
Health-related quality of life	n.a.	There are no assessable data.
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		

RM-493-033 study: single-arm, open-label phase III study, treatment phase with setmelanotide over 52 weeks; 7 patients with POMC, PCSK1 or LEPR deficiency (PPL), 5 patients with Bardet-Biedl syndrome.[a]

Mortality

Endpoint	Setmelanotide	
	N	
Overall mortality	12	No deaths occurred.

[1]Data from the dossier assessment of the G-BA (published on 2. June 2025), unless otherwise indicated.

Morbidity

Endpoint	Setmelanotide PPL[a], n=7		Setmelanotide BBS, n=5		Setmelanotide Total, N=12	
	n (%)	*MV (SD) Median (min; max)*	*n (%)*	*MV (SD) Median (min; max)*	*n (%)*	*MV (SD) Median (min; max)*
BMI (z-score)[b]						
Baseline	7 (100)	10.7 (3.84) 9.31 (6.87; 17.2)	5 (100)	4.2 (1.07) 4.36 (2.64; 5.44)	12 (100)	8.03 (4.44) 7.09 (2.64; 17.2)
Week 52: absolute change from baseline	6 (85.7)	-5.19 (1.89) -5.52 (-6.97; -2.07)	5 (100)	-1.33 (1.23) -1.07 (-3.08¸0.22)	11 (91.7)	-3.43 (2.53) -3.08 (-6.97; 0.22)
Week 52: percentage change from baseline	6 (85.7)	-54.4 (23.1) -52.3 (-83.2; -22.2)	5 (100)	-30.6 (24.2) -32.9 (-62.8; 5.13)	11 (91.7)	-43.5 (25.6) -40.2 (-83.2; 5.13)

Endpoint	Setmelanotide PPL[a], n=7	Setmelanotide BBS, n=5	Setmelanotide Total, N=12
	Patients with event n (%)	Patients with event n (%)	Patients with event n (%)
Hunger (CGIS, *presented additionally*)			
Baseline, n (%) - not hungry at all - slightly hungry - moderately hungry - very hungry	7 (100) 2 (28.6) 0 2 (28.6) 3 (42.9)	5 (100) 1 (20.0) 0 3 (60.0) 1 (20.0)	12 (100) 3 (25.0) 0 5 (41.7) 4 (33.3)
Study week 52, n (%) - not hungry at all - slightly hungry - moderately hungry - very hungry	6 (85.7) 0 4 (57.1) 2 (28.6) 0	5 (100) 0 3 (60.0%) 2 (40.0) 0	11 (91.7) 0 7 (58.3) 4 (33.3) 0

Health-related quality of life

There are no assessable data.

Side effects

Endpoint MedDRA system organ classes/ AEs of special interest	**Setmelanotide PPL[a], n=7**		**Setmelanotide BBS, n=5**		**Setmelanotide Total, N=12**	
	N	Patients with event n (%)	N	Patients with event n (%)	N	Patients with event n (%)
Total adverse events (presented additionally)	7	7 (100)	5	5 (100)	12	12 (100)
Serious adverse events (SAE)	7	0	5	0	12	0
Severe adverse events (CTCAE grade 3 or 4)	7	0	5	0	12	0
Therapy discontinuation due to adverse events	7	0	5	0	12	0
AEs of special interest (with an incidence ≥ 10%)[c]						
Hyperpigmentation of the skin	12	5 (71.4)	5	4 (80.0)	12	9 (75.0)
Haematoma at the injection site	12	1 (14.3)	5	3 (60.0)	12	4 (33.3)
Pruritus at the injection site	12	1 (14.3)	5	3 (60.0)	12	4 (33.3)
Discolouration at the injection site	12	2 (28.6)	5	1 (20.0)	12	3 (25.0)
Erythema at the injection site	12	0	5	2 (40.0)	12	2 (16.7)
Vomiting	12	4 (57.1)	5	3 (60.0)	12	7 (58.3)
Melanocytic nevus	12	3 (42.9)	5	1 (20.0)	12	4 (33.3)

a. No subject with PCSK-1 deficiency was enrolled.
b. The BMI-z was calculated using the WHO Child Growth Standard 2007 as a reference measure.
c. *Events of special interest* (ESI) according to EPAR.

Abbreviations used:
BBS = Bardet-Biedl syndrome; BMI = body mass index; CGIS = Caregiver Reported Global Impression of Severity; CTCAE = Common Terminology Criteria for Adverse Events; N = number of patients evaluated; n = number of patients with (at least one) event

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

Children 2 to < 6 years of age with genetically confirmed Bardet-Biedl syndrome, POMC, PCSK1 or LEPR deficiency for the treatment of obesity and the control of hunger

Approx. 24 – 67 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 Imcivree (active ingredient: setmelanotide) at the following publicly accessible link (last access: 04 April 2025):

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

Treatment with setmelanotide should only be initiated and monitored by specialists experienced in treating patients with obesity with underlying genetic aetiology.

4. Treatment costs

Annual treatment costs:

Children 2 to < 6 years of age with genetically confirmed Bardet-Biedl syndrome, POMC, PCSK1 or LEPR deficiency for the treatment of obesity and the control of hunger

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Children and adolescents aged 2 to 5 years, body weight < 20 kg	
Setmelanotide	€ 34,496.23
Children and adolescents aged 2 to 5 years, body weight ≥ 20 kg	
Setmelanotide	€ 34,496.23 - € 68,992.45

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 1 June 2025)

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:

Children 2 to < 6 years of age with genetically confirmed Bardet-Biedl syndrome, POMC, PCSK1 or LEPR deficiency for the treatment of obesity and the control of hunger

- No medicinal product with new active ingredients that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

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 21 August 2025.

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

Berlin, 21 August 2025

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

Prof. Hecken