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
Teprotumumab (thyroid eye disease)

From 20 August 2026

At their session on 20 August 2026, 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, information on the active ingredient teprotumumab shall be added in alphabetical order as follows:

Teprotumumab

Resolution of: 20 August 2026
Entry into force on: 20 August 2026
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 19 June 2026):

TEPEZZA is indicated in adults for the treatment of moderate to severe thyroid eye disease (TED).

Therapeutic indication of the resolution (resolution of 20 August 2026):

See therapeutic indication according to marketing authorisation.

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

a) Adults with moderate to severe thyroid eye disease in its acute stage; first-line therapy

Appropriate comparator therapy:

– Individualised therapy with selection of
  - Methylprednisolone
  - Methylprednisolone in combination with mycophenolate mofetil

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

An additional benefit is not proven.

b) Adults with moderate to severe thyroid eye disease in its acute stage who are eligible for second-line therapy

Appropriate comparator therapy:

– Individualised therapy with selection of
  - Methylprednisolone
  - Glucocorticoids in combination with orbital radiotherapy, cyclosporine or azathioprine
  - Rituximab (monotherapy)

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

An additional benefit is not proven.

c) Adults with moderate to severe thyroid eye disease in its chronic stage

Appropriate comparator therapy:

– Monitoring wait-and-see approach

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

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adults with moderate to severe thyroid eye disease in its acute stage; first-line therapy

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	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

[1] Data from the dossier assessment of the IQWiG (A26-18) and from the addendum (A26-80), unless otherwise indicated.

b) Adults with moderate to severe thyroid eye disease in its acute stage who are eligible for second-line therapy

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	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		

c) Adults with moderate to severe thyroid eye disease in its chronic stage

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	↔	No relevant difference for the benefit assessment.
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		

KBV: HZNP-TEP-403 study: RCT comparing teprotumumab with placebo

Mortality

Endpoint	Teprotumumab		Placebo		Teprotumumab vs placebo
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value[a]
Overall survival[b]					
	41	0 (0)	20	0 (0)	-

Morbidity

Endpoint	Teprotumumab		Placebo		Teprotumumab vs placebo
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value
Absence of diplopia					
	39	31 (79.5)[c]	20	16 (80.0)[c]	0.99 [0.76; 1.30][c]; > 0.999

Endpoint	Teprotumumab			Placebo			Teprotumumab vs placebo
	N[d]	Values at the start of the study MV (SD)	Mean change up to week 24 MV[e] (SE)	N[d]	Values at the start of the study MV (SD)	Mean change up to week 24 MV[e] (SE)	MD [95% CI]; p value[e]
Orbital pain (VAS)[f]							
	42	6.8 (13.7)	−5.6 (1.3)[g]	20	15.9 (27.0)	−2.4 (2.0)[h]	-3.27 [-8.07; 1.54]; 0.179

Health-related quality of life

Endpoint	Teprotumumab			Placebo			Teprotumumab vs placebo
	N	Values at the start of the study MV (SD)	Mean change up to week 24 MV[b] (SE)	N	Values at the start of the study MV (SD)	Mean change up to week 24 MV[b] (SE)	MD [95% CI]; p value[b]
GO-QoL[i]							
Visual function	42	86.4 (20.0)	7.4 (1.4)[j]	20	81.4 (18.8)	2.5 (2.0)[k]	4.94 [0.00; 9.87]; 0.050[h] SMD: 0.54 [-0.00; 1.08]
Appearance	42	46.4 (29.5)	8.2 (2.3)[j]	20	40.0 (28.6)	5.2 (3.3)[k]	2.92 [-5.25; 11.09]; 0.478

Side effects

Endpoint	Teprotumumab		Placebo		Teprotumumab vs placebo
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value
Total adverse events[l] **(presented additionally)**					
	41	33 (80.5)	20	16 (80.0)	-
Serious adverse events (SAEs)					
	41	1 (2.4)	20	1 (5.0)	0.49 [0.03; 7.40]; 0.734
Severe adverse events (CTCAE grade 3 or 4)[m]					
	41	1 (2.4)	20	1 (5.0)	0.49 [0.03; 7.40]; 0.734
Therapy discontinuation due to adverse events					
	41	1 (2.4)	20	1 (5.0)	0.49 [0.03; 7.40]; 0.734
Specific adverse events					
Hearing disorder[n] (SMQ, HLT, AEs)	41	9 (21.9)	20	2 (10.0)	2.20 [0.52; 9.23]; 0.299

a. IQWiG calculation, unconditional exact test (CSZ method).
b. The results on overall mortality are based on the data on fatal AEs.
c. IQWiG calculation; patients without diplopia (grade 0) at week 24 are classified as responders, regardless of whether they had diplopia (grade > 0) at the start of the study.
d. Number of patients considered in the effect estimate.
e. MMRM of the mean changes with value at the start of the study, visit, treatment, interaction between the visit and treatment, and interaction between the visit and the value at the start of the study as covariates; for patients without a post-baseline assessment, the change from the start of the study to the 1st data collection time point following the baseline assessment has been set to 0.
f. Lower (decreasing) values mean better symptomatology; negative effects (intervention minus comparison) mean an advantage for the intervention (scale range: 0 mm to 100 mm).
g. No post-baseline assessment was available for a maximum of 2 (5) patients.
h. At least one post-baseline assessment was available for all patients.
i. Higher (increasing) values mean better health-related quality of life; positive effects (intervention minus comparison) mean an advantage for the intervention (scale range: 0 to 100).
j. No post-baseline assessment was available for 3 (7) patients.
k. Unrounded p value < 0.05.
l. Including events that may be attributed to both side effects and symptoms of the underlying disease.
m. Operationalised as CTCAE grade ≥ 3.
n. Operationalised via the SMQ hearing disorder and the HLT hearing loss.

Abbreviations used:
CTCAE: Common Terminology Criteria for Adverse Events; GO-QoL: Graves' Ophthalmopathy Quality of Life questionnaire; HLT: high-level term; CI: confidence interval; MMRM: mixed model for repeated measures; MV: mean value; MD: mean difference; n: number of patients with (at least 1) event; N: number of patients evaluated; MedDRA: Medical Dictionary for Regulatory Activities; RCT: randomised controlled trial; RR: relative risk; SD: standard deviation; SE: standard error; SMD: standardised mean difference; SMQ: standardised MedDRA query; SAE: serious adverse event; AE: adverse event; VAS: visual analogue scale

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

a) Adults with moderate to severe thyroid eye disease in its acute stage; first-line therapy

Approx. 4,400 to 6,700 patients

b) Adults with moderate to severe thyroid eye disease in its acute stage who are eligible for second-line therapy

Approx. 2,600 to 4,000 patients

c) Adults with moderate to severe thyroid eye disease in its chronic stage

Approx. 11,200 to 17,000 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 Tepezza (active ingredient: teprotumumab) at the following publicly accessible link (last access: 3 June 2026):

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

Treatment with teprotumumab should only be initiated and monitored by specialists who are experienced in the treatment of patients with thyroid eye disease.

A clinical response is expected after 8 treatment doses. If no response is achieved with this treatment regimen, no further doses should be administered.

In accordance with the EMA requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients (including patient guideline). The training material contains, in particular, information and warnings regarding hearing disorders and for women of reproductive age.

4. Treatment costs

Annual treatment costs:

A period of one year is assumed for calculating the costs of off-label use of mycophenolate mofetil, cyclosporine, azathioprine and rituximab.

a) Adults with moderate to severe thyroid eye disease in its acute stage; first-line therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Teprotumumab Additionally required SHI services: Total:	€ 209,792.70 € 55.80 € 209,848.50
Appropriate comparator therapy:	
Methylprednisolone (monotherapy)	
Methylprednisolone	€ 227.40 - € 463.33
Methylprednisolone in combination with mycophenolate mofetil	
Methylprednisolone	€ 227.40
Mycophenolate mofetil	€ 1,129.92
Methylprednisolone + mycophenolate mofetil	€ 1,357.32

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 June 2026)

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Teprotumumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	8	8	€ 800

b) <u>Adults with moderate to severe thyroid eye disease in its acute stage who are eligible for second-line therapy</u>

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Teprotumumab Additionally required SHI services: Total:	€ 209,792.70 € 55.80 € 209,848.50
Appropriate comparator therapy:	
Methylprednisolone (monotherapy)	
Methylprednisolone	€ 227.40 - € 463.40
Glucocorticoids in combination with orbital radiotherapy	
Methylprednisolone	€ 117.96 - € 227.40
Methylprednisolone followed by prednisone	€ 227.40
Prednisone	Different from patient to patient
Orbital radiotherapy	€ 836.09 - € 1,656.89
Glucocorticoids in combination with cyclosporine	
Prednisone	€ 52.65 - € 66.57
Cyclosporine	Different from patient to patient
Glucocorticoids in combination with azathioprine	
Glucocorticoids (prednisolone)	€ 80.80
Azathioprine	€ 210.20 - € 420.40
Prednisolone + azathioprine	€ 291.00 - € 501.20
Rituximab (monotherapy)	
Rituximab	€ 364.78 - € 1,691.39

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 June 2026)

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Teprotumumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	8	8	€ 800
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	1	€ 100

c) <u>Adults with moderate to severe thyroid eye disease in its chronic stage</u>

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Teprotumumab Additionally required SHI services: Total:	€ 209,792.70 € 55.80 € 209,848.50
Appropriate comparator therapy:	
Monitoring wait-and-see approach	Non-quantifiable

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 June 2026)

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Teprotumumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	8	8	€ 800

II. The resolution will enter into force on the day of its publication on the G-BA website on 20 August 2026.

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

Berlin, 20 August 2026

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

Dr Optendrenk