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)
Nintedanib (new therapeutic indication: clinically significant, progressive fibrosing interstitial lung diseases, 6 to < 18 years)

of 7 August 2025

At their session on 7 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. 4 to the information on the benefit assessment of Nintedanib in accordance with the resolution of 4 February 2021:

Nintedanib

Resolution of: 7 August 2025
Entry into force on: 7 August 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 12 February 2025):

Ofev is indicated in children and adolescents from 6 to 17 years old for the treatment of clinically significant, progressive fibrosing interstitial lung diseases (ILDs).

Therapeutic indication of the resolution (resolution of 7 August 2025):

See new therapeutic indication according to marketing authorisation.

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

Children and adolescents from 6 to 17 years old with clinically significant, progressive fibrosing interstitial lung diseases (ILDs)

Appropriate comparator therapy:

Best supportive care

Extent and probability of the additional benefit of nintedanib compared to the best supportive care:

An additional benefit is not proven.

Study results according to endpoints:[1]

Children and adolescents from 6 to 17 years old with clinically significant, progressive fibrosing interstitial lung diseases (ILDs)

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A25-30) unless otherwise indicated.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No deaths occurred.
Morbidity	↔	No relevant differences for the benefit assessment.
Health-related quality of life	↔	No relevant differences for the benefit assessment.
Side effects	↔	No relevant differences 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		

InPedILD study: Nintedanib vs placebo

Mortality

Endpoint	Nintedanib + BSC		Placebo + BSC		Nintedanib + BSC vs placebo + BSC
	N	Median survival time in months [95% CI] *Patients with event n (%)*	N	Median survival time in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value
Overall mortality[a] (at week 24)					
	26	n.r. *0 (0)*	13	n.r. *0 (0)*	-

Morbidity

Endpoint	Nintedanib + BSC			Placebo + BSC			Nintedanib + BSC vs placebo + BSC
	N	Median survival time in months [95% CI] *Patients with event n (%)*		N	Median survival time in months [95% CI] *Patients with event n (%)*		HR [95% CI] p value
Acute exacerbation[b] or death							
	26	n.r. *1 (3.9)*		13	n.r. *0 (0)*		n.d.[c]
		Values at the start of the study MV (SD)	Change at week 24 MV (SE)		Values at the start of the study MV (SD)	Change at week 24 MV (SE)	MD [95% CI]; p value
(Physical) resilience (6MWT)							
	No suitable data						

Health-related quality of life

Endpoint	Nintedanib + BSC		Placebo + BSC		Nintedanib + BSC vs placebo + BSC
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value[d]
PedsQL – deterioration by ≥ 15 points at week 24[e]					
	26	0 (0)	13	1 (9.1)	n.c.[f]

Side effects

Endpoint	Nintedanib + BSC		Placebo + BSC		Nintedanib + BSC vs placebo + BSC
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value[d]
Total adverse events *(presented additionally)*					
	26	22 (84.6)	13	11 (84.6)	-

Endpoint	Nintedanib + BSC		Placebo + BSC		Nintedanib + BSC vs placebo + BSC
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI] p value[d]
Serious adverse events (SAE)					
	26	1 (3.8)	13	1 (7.7)	0.5 [0.03; 7.37]; 0.734
Therapy discontinuation due to adverse events					
	26	2 (7.7)	13	0 (0)	2.59 [0.13; 50.38]; 0.397
Hepatobiliary disorders (SOC, SAEs)					
	26	0 (0)	13	0 (0)	n.c.
Gastrointestinal disorders (SOC, AEs)					
	26	22 (84.6)	13	11 (84.6)	1.00 [0.75; 1.33]; > 0.999
Diarrhoea (PT, AEs)					
	26	10 (38.5)	13	2 (15.4)	2.50 [0.64; 9.78]; 0.163

a. The results on overall mortality are based on the information on fatal AEs or the vital status surveys in the eCRF.
b. Acute exacerbations were defined as a significant deterioration of the respiratory tracts over a four-week period that required a change in regular treatment, based on two or more of the following criteria: Increase in respiratory rate by ≥ 20%, deterioration or development of dyspnoea, deterioration or development of abnormalities in the chest radiograph, increase in oxygen requirement to achieve individual baseline saturation (at rest or in case of physical burden), need for supplemental ventilatory support (in addition to oxygen), deterioration of spirometry in children and adolescents who are able to perform the tests (≥ 10% from baseline value of vital capacity), decreased tolerance to physical burden.
c. Due to the low number of events, the pharmaceutical company refrains from calculations of the HR (including 95% CI) and p value
a. Unless otherwise stated: IQWiG calculation of RR, CI (asymptotic) and p value (unconditional exact test, CSZ method according to [25]); in the case of 0 events in one study arm, the correction factor 0.5 was used in both study arms when calculating the effect and CI.
e. A decrease in score by ≥ 15 points compared to the start of study is considered clinically relevant deterioration (scale range: 0 to 100).
f. Log-link Poisson model with robust variance estimation with the covariates baseline value (continuous), age group (6 to < 12 years, 12 to < 18 years) and treatment group

Abbreviations used:
6MWT = 6-minute walk test; BSC = best supportive care; eCRF = electronic Case Report Form; HR = hazard ratio; n.d. = no data available; CI = confidence interval; MD = mean difference; MV = mean value; n = number of patients with (at least 1) event; N = number of patients evaluated; n.r. = not reached; PedsQL = Paediatric Quality of Life Questionnaire; PT = preferred term; RR = relative risk; SD = standard deviation; SE = standard error; SOC = system organ class; SAE = serious adverse event; AE = adverse event

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

Children and adolescents from 6 to 17 years old with clinically significant, progressive fibrosing interstitial lung diseases (ILDs)

Approx. 1 – 35 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 Ofev (active ingredient: nintedanib) at the following publicly accessible link (last access: 3 June 2025):

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

Treatment should be initiated and monitored only after involvement of a multidisciplinary team (physicians, radiologists, pathologists) experienced in the diagnosis and treatment of fibrosing interstitial lung diseases (ILDs).

4. Treatment costs

Annual treatment costs:

Children and adolescents from 6 to 17 years old with clinically significant, progressive fibrosing interstitial lung diseases (ILDs)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Nintedanib	€ 23,393.95 - € 34,999.49
Best supportive care	Different from patient to patient
Appropriate comparator therapy:	
Best supportive care	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 July 2025)

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:

Children and adolescents from 6 to 17 years old with clinically significant, progressive fibrosing interstitial lung diseases (ILDs)

- No medicinal product with new active ingredients that can be used in a combination therapy and 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 7 August 2025.

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

Berlin, 7 August 2025

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

Prof. Hecken