

**Resolution
by the Federal Joint Committee
on an amendment to the Pharmaceutical Directive (AM-RL):
Appendix XII – Resolutions on the benefit assessment of pharmaceuticals with new active ingredients,
in accordance with the German Social Code, Book Five (SGB V), section 35a
Boceprevir
from 1 March 2012**

In its session on 1 March 2012, the Federal Joint Committee resolved to amend the Pharmaceutical Directive (AM-RL), version published 18 December 2008/22 January 2009 (Federal Gazette, number 49a of 31 March 2009), last amended on 15 December 2011 (Federal Gazette, 2012, page 786), as follows:

I.

Appendix XII shall be amended in alphabetical order to include the active ingredient boceprevir:

Boceprevir

Therapeutic indication:

Victrelis® is indicated for the treatment of chronic hepatitis C (CHC) genotype 1 infection, in combination with peginterferon alfa and ribavirin, in adult patients with compensated liver disease who are previously untreated or who have failed previous therapy.

1. Additional benefit of the pharmaceutical over appropriate comparator

a) In combination with peginterferon + ribavirin as compared to peginterferon + ribavirin in previously untreated patients with chronic hepatitis C viral (cHCV) genotype 1 infection

Appropriate comparator: peginterferon plus ribavirin

Extent and probability of additional benefit over peginterferon plus ribavirin:

Indication of an additional benefit of boceprevir; extent not quantifiable

Study results according to endpoints¹:

	Effect estimates [95% CI] BOC+PegIFN/RBV vs. PegIFN/RBV	Incident rate BOC+PegIFN/RBV vs. PegIFN/RBV/ absolute risk reduction (ARR) ²	p-value
SVR	RR 1.68 [1.44; 1.96]	63.3% vs. 37.7% ARR = 25.6%	p < 0.001
Health-related quality of life	No applicable data available	–	–
Overall mortality	RR 0.25 [0.03; 2.20]	< 1% vs. 1%	p = 0.195
Anaemia	RR 1.68 [1.39; 2.03]	49% vs. 29% ARR = -20%	p < 0.001
Psychiatric incidents	RR 0.94 [0.83; 1.06]	55% vs. 59%	p = 0.312
Infection	RR 1.01 [0.87; 1.16]	51% vs. 50%	p = 0.934
AE	RR 1.01 [0.99; 1.03]	99% vs. 98%	p = 0.22
SAE	RR 1.34 [0.86; 2.08]	11% vs. 9%	p = 0.22
Termination due to AE	RR 0.78 [0.54; 1.12]	12% vs. 16%	p = 0.20

¹ Data from the benefit assessment conducted by the Institute for Quality and Efficiency in Health Care (IQWiG), page 21 (Sprint-2)

² Figures given only in cases with significant differences; negative ARR figures are in favor of appropriate comparator (PegIFN/RBV)

b) In combination with peginterferon + ribavirin as compared to peginterferon + ribavirin in previously treated patients with cHCV genotype 1 infection

Appropriate comparator: peginterferon plus ribavirin

Extent and probability of additional benefit over peginterferon plus ribavirin:

Indication of an additional benefit of boceprevir; extent not quantifiable

Study results according to endpoints¹:

	Effect estimates [95% CI] BOC+PegIFN/RBV vs. PegIFN/RBV	Incident rate BOC+PegIFN/RBV vs. PegIFN/RBV absolute risk reduction (ARR) ²	p-value
SVR	RR 2.76 [1.78; 4.29]	58.6% vs. 21.3% ARR = 37.3%	p < 0.001
Health-related quality of life	No applicable data available	–	–
Overall mortality	Incalculable	0.6% vs. 0%	p = 0.595
Anaemia	RR 2.10 [1.35; 3.47]	43% vs. 20% ARR = -23%	p < 0.001
Psychiatric incidents	RR 1.09 [0.81; 1.46]	48% vs. 44%	p = 0.623
Infection	RR 0.89 [0.69; 1.14]	50% vs. 56%	p = 0.402
AE	RR 1.03 [0.98; 1.08]	99% vs. 96%	p = 0.34
SAE	RR 1.98 [0.68; 5.72]	10% vs. 5%	p = 0.23
Termination due to AE	RR 3.21 [0.74; 13.88]	8% vs. 3%	p = 0.15

¹ Data from the benefit assessment conducted by the Institute for Quality and Efficiency in Health Care (IQWiG), page 21 (Respond-2)

² Figures given only in cases with significant differences; negative ARR figures are in favor of appropriate comparator (PegIFN/RBV)

2. Number of patients and criteria for defining patients eligible for treatment

a) In combination with peginterferon + ribavirin as compared to peginterferon + ribavirin in previously untreated patients with chronic hepatitis C viral (cHCV) genotype 1 infection

Number: approx. 12,000

(diagnosed, previously untreated patients with chronic hepatitis C virus infection)

b) In combination with peginterferon + ribavirin as compared to peginterferon + ribavirin in previously treated patients with cHCV genotype 1 infection

Number: approx. 34,000

(diagnosed, previously treated patients with chronic hepatitis C virus infection)

3. Requirements for quality-assured administration

The specifications outlined in the product information are to be followed.

4. Costs of treatment

("Lauer-Taxe", effective 15 February 2012)

a) In combination with peginterferon + ribavirin as compared to peginterferon + ribavirin in previously untreated patients with chronic hepatitis C viral (cHCV) genotype 1 infection

Duration of treatment:

Chart: previously untreated patients (without cirrhosis) with chronic hepatitis C virus (cHCV) infection who respond early to treatment

Population/ patient group	Description of therapy	Mode of treatment	Number of treatments per patient per year	Duration per treatment (days)	Duration of treatment per patient per year
Previously untreated, without cirrhosis (Early responders ¹)	Boceprevir + ribavirin + peginterferon	3 x daily 2 x daily 1 x weekly	1 treatment cycle of 28 weeks	168 196 28	168 196 28
		4 weeks ribavirin + peginterferon, then 24 weeks boceprevir + ribavirin + peginterferon			
Previously untreated (Low initial viral load ^{2,3})	Ribavirin + peginterferon	2 x daily 1 x weekly	1 treatment cycle of 24 weeks	168 24	168 24
		24 weeks ribavirin + peginterferon			

¹ HCV-RNA test: treatment week 8, 24: undetectable

² Genotype 1 patients with low initial viral load (LVL) (≤ 800000 IU/ml) who test HCV-RNA negative by week 4 and remain negative until week 24

³ An overall therapy duration of 24 weeks can lead to increased risk of relapse. For these patients, tolerance of the combination therapy and additional prognostic factors like degree of fibrosis should be taken into consideration.

Chart: previously untreated patients without cirrhosis with chronic hepatitis C virus (cHCV) infection who do not respond early to treatment; previously untreated patients with cirrhosis

Population/ patient group	Description of therapy	Mode of treatment	Number of treatments per patient per year	Duration per treatment (days) ¹	Duration of treatment per patient per year
Previously untreated, without cirrhosis	Boceprevir + ribavirin + peginterferon	3 x daily 2 x daily 1 x weekly	1 treatment cycle of 48 weeks	224 336 48	224 336 48
		4 weeks ribavirin + peginterferon, then 32 weeks boceprevir + ribavirin + peginterferon, then 12 weeks ribavirin + peginterferon			
Previously untreated, with cirrhosis	Boceprevir + ribavirin + peginterferon	3 x daily 2 x daily 1 x weekly	1 treatment cycle of 48 weeks	308 336 48	308 336 48
		4 weeks ribavirin + peginterferon, then 44 weeks boceprevir + ribavirin + peginterferon,			
Previously untreated	Ribavirin + peginterferon	2 x daily 1 x weekly	1 treatment cycle of 48 weeks	336 48	336 48
		48 weeks ribavirin + peginterferon			

¹ Termination rules in accordance with Victrelis® product information were not represented.

Consumption:

Chart: previously untreated patients (without cirrhosis) with chronic hepatitis C virus (cHCV) infection who respond early to treatment

Population/ patient group	Description of therapy	Strength	Number/amount per pack ^{2,3}	Average annual consumption ²
Previously untreated, without cirrhosis (Early responders)	Boceprevir + ribavirin + peginterferon	2400mg (3 x [4 x 200mg]) 1000mg ¹ (1 x [2 x 200mg], 1 x [3 x 200mg]) 180 micrograms	336 tablets 168 tablets 12 pre-filled syringes (180 µg each)	2,016 tablets 980 tablets 28 pre-filled syringes
Previously untreated (Low initial viral load)	Ribavirin + peginterferon	1000mg ¹ (1 x [2 x 200mg], 1 x [3 x 200mg]) 180 micrograms	168 tablets 12 pre-filled syringes (180 µg each)	840 tablets 24 pre-filled syringes

¹ Body weight < 75 kg

² Tablets or pre-filled syringes

³ Largest pack

Chart: previously untreated patients (without cirrhosis) with chronic hepatitis C virus (cHCV) infection who do not respond early
previously untreated patients with cirrhosis

Population/ patient group	Description of therapy	Strength	Number/amount per pack ^{2,3}	Average annual consumption ²
Previously untreated, without cirrhosis	Boceprevir + ribavirin + peginterferon	2400mg (3 × [4 × 200mg]) 1000mg ¹ (1 × [2 × 200mg], 1 × [3 × 200mg]) 180 micrograms	336 tablets 168 tablets 12 pre-filled syringes (180 µg each)	2,688 tablets 1,680 tablets 48 pre-filled syringes
Previously untreated, with cirrhosis	Boceprevir + ribavirin + peginterferon	2,400mg (3 × [4 × 200mg]) 1000mg ¹ (1 × [2 × 200mg], 1 × [3 × 200mg]) 180 micrograms	336 tablets 168 tablets 12 pre-filled syringes (180 µg each)	3,696 tablets 1,680 tablets 48 pre-filled syringes
Previously untreated	Ribavirin + peginterferon	1000mg ¹ (1 × [2 × 200mg], 1 × [3 × 200mg]) 180 micrograms	168 tablets 12 pre-filled syringes (180 µg each)	1,680 tablets 48 pre-filled syringes

¹Body weight < 75 kg

²Tablets or pre-filled syringes

³Largest pack

Costs:

Cost of pharmaceutical:

Chart: previously untreated patients with chronic hepatitis C virus (CHCV) infection who respond/do not respond early to treatment

Population/ patient group	Description of therapy	Cost (pharmacy retail price)	Cost after legally mandated rebates
Previously untreated, with/without cirrhosis (Early responders and non-early responders)	Boceprevir (Victrelis®200mg) (336 tablets)	€3,979.07	€3,465.02 Rebate in accordance with SGB V, section 130, paragraph 1: €2.05 Rebate in accordance with SGB V, section 130a, paragraph 1a: €512.00
	Ribavirin (Copegus®200mg) (168 tablets)	€1,003.72	€821.50 Rebate in accordance with SGB V, section 130, paragraph 1: €2.05 Rebate in accordance with SGB V, section 130a, paragraph 1a: €180.17
	Peginterferon (Pegasys®180µg) (12 pre-filled syringes)	€3,361.81	€2,820.48 Rebate in accordance with SGB V, section 130, paragraph 1: €2.05 Rebate in accordance with SGB V, section 130a, paragraph 1a: €539.28
	Peginterferon (Pegasys®180µg) (4 pre-filled syringes)	€1,146.85	€965.04 Rebate in accordance with SGB V, section 130, paragraph 1: €2.05 Rebate in accordance with SGB V, section 130a, paragraph 1a: €179.76
Previously untreated, with cirrhosis	Ribavirin (Copegus®200mg) (168 tablets)	€1,003.72	€821.50 Rebate in accordance with SGB V, section 130, paragraph 1: €2.05 Rebate in accordance with SGB V, section 130a, paragraph 1a: €180.17
	Peginterferon (Pegasys®180µg) (12 pre-filled syringes)	€3,361.81	€2,820.48 Rebate in accordance with SGB V, section 130, paragraph 1: €2.05 Rebate in accordance with SGB V, section 130a, paragraph 1a: €539.28
Previously untreated (Low and not low initial viral load)	Ribavirin (Copegus®200mg) (168 tablets)	€1,003.72	€821.50 Rebate in accordance with SGB V, section 130, paragraph 1: €2.05 Rebate in accordance with SGB V, section 130a, paragraph 1a: €180.17
	Peginterferon (Pegasys®180µg) (12 pre-filled syringes)	€3,361.81	€2,820.48 Rebate in accordance with SGB V, section 130, paragraph 1: €2.05 Rebate in accordance with SGB V, section 130a, paragraph 1a: €539.28

Costs for additional, necessary statutory health insurance (SHI) benefits:

Chart: previously untreated patients with chronic hepatitis C virus (CHCV) infection who respond/do not respond early to treatment

Population/ patient group	Description of therapy	Description of additional SHI expense item	Number of additional necessary SHI expense items per episode, cycle, etc.	Number of additional, necessary SHI expense items per patient per year	Cost per unit
Previously untreated, without cirrhosis (Early responders and	Boceprevir + ribavirin + peginterferon	Test for HCV- RNA levels	1 x in treatment week 8	1 x	€89.50
Previously untreated, with cirrhosis	Boceprevir + ribavirin + peginterferon	none	–	–	–
Previously untreated (Low and not low initial viral load)	Ribavirin + peginterferon	none	–	–	–

Annual treatment costs:

Chart: previously untreated patients (without cirrhosis) with chronic hepatitis C virus (CHCV) infection who respond early to treatment

Population/patient group	Description of therapy	Annual treatment costs per patient
Previously untreated, without cirrhosis (Early responders)	Boceprevir + ribavirin + peginterferon	€32,414.62 (Duration of treatment 28 weeks)
Previously untreated (Low initial viral load)	Ribavirin + peginterferon	€9,748.46 (Duration of treatment 24 weeks)

Chart: previously untreated patients without cirrhosis with chronic hepatitis C virus (cHCV) infection who do not respond early to treatment; previously untreated patients with cirrhosis

Population/patient group	Description of therapy	Annual treatment costs per patient
Previously untreated, without cirrhosis	Boceprevir + ribavirin + peginterferon	€44,020.58 (Duration of treatment 48 weeks)
Previously untreated, with cirrhosis	Boceprevir + ribavirin + peginterferon	€54,326.14 (Duration of treatment 48 weeks)
Previously untreated (not low initial viral load)	Ribavirin + peginterferon	€19,496.92 (Duration of treatment 48 weeks)

b) In combination with peginterferon + ribavirin as compared to peginterferon + ribavirin in previously treated patients with cHCV genotype 1 infection

Duration of treatment:

Population/ patient group	Description of therapy	Mode of treatment	Number of treatments per patient per year	Duration per treatment (days) ¹	Treatment days per patient per year
Previously treated, without cirrhosis ²	Boceprevir + ribavirin + peginterferon	3 × daily 2 × daily 1 × weekly	1 treatment cycle of 48 weeks	224 336 48	224 336 48
		4 weeks ribavirin + peginterferon, then 32 weeks boceprevir + ribavirin + peginterferon, then 12 weeks ribavirin + peginterferon			
Previously treated, with cirrhosis; non-responders	Boceprevir + ribavirin + peginterferon	3 × daily 2 × daily 1 × weekly	1 treatment cycle of 48 weeks	308 336 48	308 336 48
		4 weeks ribavirin + peginterferon, then 44 weeks boceprevir + ribavirin + peginterferon			
Previously treated	Ribavirin + peginterferon ³	2 × daily 1 × weekly	1 treatment cycle of 48 weeks	336 48	336 48
		48 weeks ribavirin + peginterferon			
Previously treated	Ribavirin + peginterferon ⁴	2 × daily 1 × weekly	1 treatment cycle of 72 weeks	504 72	504 72 (in one treatment cycle of 72 weeks)
		72 weeks ribavirin + peginterferon			

¹Termination rules in accordance with Victrelis[®] product information were not represented.

²Patients who did not respond to previous treatment with interferon and ribavirin and/or have relapsed

³Therapy for previously treated patients with the combination of Rebetol[®] and PegIntron[®]: duration of therapy 48 weeks according to product information

⁴Therapy for previously treated patients with the combination of Copegus[®] and Pegasys[®]: duration of therapy 72 weeks according to product information

Consumption:

Population/ patient group	Description of therapy	Strength (mg)	Number/amount per pack ^{2,3}	Average annual consumption ²
Previously treated, without cirrhosis	Boceprevir + ribavirin + peginterferon	2400mg (3 × [4 × 200mg]) 1000mg ¹ (1 × [2 × 200mg], 1 × [3 × 200mg]) 180 micrograms	336 tablets 168 tablets 12 pre-filled syringes (180 µg each)	2688 tablets 1,680 tablets 48 pre-filled syringes
Previously treated, with cirrhosis; non-responders	Boceprevir + ribavirin + peginterferon	2,400mg (3 × [4 × 200mg]) 1000mg ¹ (1 × [2 × 200mg], 1 × [3 × 200mg]) 180 micrograms	336 tablets 168 tablets 12 pre-filled syringes (180 µg each)	3,696 tablets 1,680 tablets 48 pre-filled syringes
Previously treated	Ribavirin + peginterferon	1000mg ¹ (1 × [2 × 200mg], 1 × [3 × 200mg]) 100 micrograms ¹	168 tablets 12 pre-filled syringes (100 µg each)	1,680 tablets 48 pre-filled syringes
Previously treated	Ribavirin + peginterferon	1000mg ¹ (1 × [2 × 200mg], 1 × [3 × 200mg]) 180 micrograms	168 tablets 12 pre-filled syringes (180 µg each)	2,520 tablets 72 pre-filled syringes (in one treatment cycle of 72 weeks)

¹Body weight < 75 kg²Tablets or pre-filled syringes³Largest pack

Costs:

Cost of pharmaceutical:

Population/ patient group	Description of therapy	Cost (pharmacy retail price ¹)	Cost after legally mandated rebates
Previously treated with/without cirrhosis; non-responders	Boceprevir (Victrelis®200mg)	€3,979.07	€3,465.02 Rebate in accordance with SGB V, section 130, paragraph 1: €2.05 Rebate in accordance with SGB V, section 130a, paragraph 1a: €512.00
	Ribavirin (Copegus®200mg)	€1,003.72	€821.50 Rebate in accordance with SGB V, section 130, paragraph 1: €2.05 Rebate in accordance with SGB V, section 130a, paragraph 1a: €180.17
	Peginterferon (Pegasys®180µg)	€3,361.81	€2,820.48 Rebate in accordance with SGB V, section 130, paragraph 1: €2.05 Rebate in accordance with SGB V, section 130a, paragraph 1a: €539.28
Previously treated	Ribavirin (Copegus®200mg)	€1,003.72	€821.50 Rebate in accordance with SGB V, section 130, paragraph 1: €2.05 Rebate in accordance with SGB V, section 130a, paragraph 1a: €180.17
	Peginterferon (Pegasys®180µg)	€3,361.81	€2,820.48 Rebate in accordance with SGB V, section 130, paragraph 1: €2.05 Rebate in accordance with SGB V, section 130a, paragraph 1a: €539.28
	Ribavirin (Rebetol®200mg)	€1,035.68	€903.89 Rebate in accordance with SGB V, section 130, paragraph 1: €2.05 Rebate in accordance with SGB V, section 130a, paragraph 1a: €129.74
	Peginterferon (PegIntron®100µg)	€3,311.56	€2,809.22 Rebate in accordance with SGB V, section 130, paragraph 1: €2.05 Rebate in accordance with SGB V, section 130a, paragraph 1a: €500.29

¹Largest pack

Costs for additional, necessary statutory health insurance (SHI) benefits:

Population/ patient group	Description of therapy	Description of additional SHI expense item	Number of additional, necessary SHI expense items per episode, cycle, etc.	Number of additional, necessary SHI expense items per patient per year	Cost per unit
Previously treated, without cirrhosis	Boceprevir + ribavirin + peginterferon	Test for HCV- RNA levels	1 x in treatment week 8	1 x	€89.50
Previously treated, with cirrhosis; non-responders	Boceprevir + ribavirin + peginterferon	none	–	–	–
Previously treated	Ribavirin + peginterferon	none	–	–	–

Annual treatment costs:

Population/patient group	Description of therapy	Annual treatment costs per patient
Previously treated, without cirrhosis	Boceprevir + ribavirin + peginterferon	€44,020.58 (Duration of treatment 48 weeks)
Previously treated, with cirrhosis; non-responders	Boceprevir + ribavirin + peginterferon	€54,326.14 (Duration of treatment 48 weeks)
Previously treated	Ribavirin + peginterferon	€20,275.78 (Duration of treatment 48 weeks)
Previously treated	Ribavirin + peginterferon	€29,245.38 (Duration of treatment 72 weeks)

II.

This resolution takes effect on the day of its publication in the internet on the website of the Federal Joint Committee on 1 March 2012. The justification for this resolution will be published on the website of the Federal Joint Committee at www.g-ba.de.

Berlin, 1 March 2012

The Federal Joint Committee in
accordance with SGB V,
section 91
The Chair
Hess