Justification

Gemeinsamer Bundesausschuss

to 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 Fidaxomicin (New Therapeutic Indication: Clostridioides Difficile Infection, Children and Adolescents)

of 3 September 2020

Contents

1. Legal basis

According to Section 35a, paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of reimbursable medicinal products with new active ingredients. This includes in particular the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical trials the pharmaceutical company has conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. Approved therapeutic indications,
2. Medical benefit,
3. Additional medical benefit in relation to the appropriate comparator therapy,
4. Number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. Treatment costs for statutory health insurance funds,
6. Requirements for a quality-assured application.

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a, paragraph 3 SGB V, the G-BA decides on the benefit assessment within three months of its publication. The resolution is to be published on the internet and forms part of the Pharmaceuticals Directive.

2. Key points of the resolution

The active ingredient fidaxomicin (Dificlir™) was listed for the first time on 15 January 2013 in the “LAUER-TAXE®”, the extensive German registry of available drugs and their prices.

On 14 February 2020, fidaxomicin received the marketing authorisation for a new therapeutic indication classified as a major variation of Type 2 according to Annex 2, number 2a to Regulation (EC) No. 1234/2008 of the Commission from 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12 December 2008, p. 7).

On 11 March 2020, the pharmaceutical company submitted a dossier in accordance with Section 4, paragraph 3, number 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient fidaxomicin with the new therapeutic indication in due time (i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication (treatment of *Clostridioides difficile* infections (CDI) also known as *C. difficile*-associated diarrhoea (CDAD) in children and adolescents).

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 15 June 2020 on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of fidaxomicin compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements

submitted in the written statement and oral hearing procedure. In order to determine the extent of the additional benefit, the G-BA has assessed the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5, Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of fidaxomicin.

In the light of the above and taking into account the statements received and the oral hearing, the G-BA has arrived at the following assessment:

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

2.1.1 Approved therapeutic indication of fidaxomicin (Dificlir™) in accordance with the product information

Dificlir is indicated for the treatment of Clostridioides difficile infections (CDI) also known as C. difficile-associated diarrhoea (CDAD) in adults and paediatric patients from birth to < 18 years of age (see section 4.2 and 5.1).

Consideration should be given to official guidelines on the appropriate use of antibacterial agents.

This resolution relates exclusively to children and adolescents under 18 years of age.

Dificlir with the active ingredient fidaxomicin is available in various dosage forms: Film-coated tablets and granules for oral suspension. Fidaxomicin granules for the preparation of an oral suspension are currently not available on the German market. The findings of this resolution shall nevertheless apply to both approved dosage forms.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a) Patients < 18 years of age with mild courses of *Clostridioides difficile*-associated diarrhoea requiring treatment

metronidazole or vancomycin

b) Patients < 18 years of age with severe and/or recurrent courses of *Clostridioides difficile*-associated diarrhoea

vancomycin

Criteria according to Chapter 5, Section 6 of the Rules of Procedure of the G-BA:

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication according to the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

[1] General Methods, Version 5.0 dated 10 July 2017. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen [Institute for Quality and Efficiency in Health Care], Cologne.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5, Section 6, paragraph 3 VerfO:

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal applications or non-medicinal treatments for which the patient-relevant benefit has already been determined by the Federal Joint Committee shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

Justification based on the criteria set out in Chapter 5, Section 6, paragraph 3 VerfO:

On 1. In the therapeutic indication, the following medicinal product (antibiotics) are approved for the treatment of CDI in patients under 18 years of age: metronidazole, vancomycin, and teicoplanin. The antibiotic teicoplanin is indicated as an alternative treatment for CDI and is therefore not considered a regular comparator therapy.

On 2. In the present therapeutic indication, the application of a donor stool suspension (stool transplantation) is generally considered as a non-medicinal therapy option.

On 3. There are no resolutions in the aforementioned therapeutic indication. In the therapeutic indication CDI in adult patients, there are two resolutions of the G-BA on the benefit assessment of medicinal products with new active ingredients according to § 35a SGB V. For fidaxomicin (resolution of 4 July 2013), there is proof of a considerable additional benefit in adult patients with severe and/or recurrent CDI disease and no additional benefit in adult patients with mild CDI disease requiring treatment. On the other hand, for bezlotoxumab (resolution of 20 September 2018) for the prevention of recurrence of a CDI in adult patients with a high risk of recurrence, there was an indication of a minor additional benefit.

On 4. The generally accepted state of medical knowledge was illustrated by systematic research for guidelines and reviews of clinical studies in the present indication and is presented in the “Research and synopsis of the evidence to determine the appropriate comparator therapy in accordance with Section 35a SGB V”. Within the scope of the evidence search, it was determined that the evidence available for the present therapeutic indication is limited overall. For lack of high-quality evidence, the only source used was the guideline of McDonald et al. (2018), which provides therapeutic recommendations for the treatment of Clostridioides difficile infections in adults and children. No other relevant or methodologically adequate reviews or guidelines were identified.
There is only limited evidence for the efficacy of a stool transplantation. There is also a lack of established standardisation of the method. The use of stool transplantation as a non-medicinal therapy is not regularly considered in this therapeutic indication because it is mentioned only as an option if standard antibiotic therapy for multiple relapses fails. Stool transplantation is therefore not part of the appropriate comparator therapy.

For the approved medicinal product, the present US guideline (McDonald *et al.*, 2018) contains different recommendations for the treatment of CDI in patients under 18 years of age depending on the severity and recurrence of the disease. For the treatment of CDI patients under 18 years of age with mild disease courses requiring treatment, the guideline recommends therapy with metronidazole or vancomycin. Both active ingredients are considered equally appropriate; no prioritisation is made. For the

treatment of patients under 18 years of age with severe and/or recurrent CDI disease, the guideline recommends therapy with vancomycin.

Against this background, the G-BA considers it justified to follow the recommendations of the guideline and identify metronidazole or vancomycin as an appropriate comparator therapy for fidaxomicin for the treatment of CDI in patients < 18 years depending on the severity and course of the disease for patients with mild disease courses requiring treatment of CDI as well as vancomycin as an appropriate comparator therapy for patients with severe and/or recurrent CDI. In principle, guidelines on the appropriate use of antibiotics should be taken into account.

The findings in Annex XII do not restrict the scope of treatment required to fulfil the medical treatment contract.

2.1.3 Extent and probability of the additional benefit

In summary, the additional benefit of fidaxomicin is assessed as follows:

For the assessment of the additional benefit, the pharmaceutical company presents in the dossier the single-blind, parallel, randomised, controlled SUNSHINE study, which compares fidaxomicin with vancomycin. This study includes patients with mild treatment-requiring as well as severe and/or recurrent disease courses of a confirmed CDI. CDI diagnosis included the detection of Toxin A, Toxin B, or toxigenic Clostridioides difficile strains in stool within 72 hours prior to randomisation. On the other hand, patients < 2 years had to have watery diarrhoea and patients ≥ 2 years had to have at least 3 unformed bowel movements within 24 hours before screening.

A total of 148 patients were randomised and assigned to treatment with fidaxomicin (N = 100) or vancomycin (N = 48) at a ratio of 2:1. The stratification factor was age (< 2 years, ≥ 2 to < 6 years, ≥ 6 to < 12 years, and ≥ 12 to < 18 years). Patients were assigned post hoc to the sub-population with mild disease course requiring treatment or the sub-population with severe and/or recurrent disease course. Of these patients, 66 are relevant for the assessment of patient population a) with mild disease course requiring treatment and 82 for the assessment of patient population b) with severe and/or recurrent disease course.

The primary endpoint was confirmed clinical response; patient-relevant secondary endpoints were further endpoints on morbidity and side effects. All endpoints were observed for 30 days after completion of treatment.

a) <u>Patients < 18 years of age with mild courses of Clostridioides difficile-associated diarrhoea requiring treatment</u>

For patients < 18 years of age with mild courses of Clostridioides difficile-associated diarrhoea requiring treatment, the additional benefit is not proven.

Justification:

<u>Extent and probability of the additional benefit</u>

<u>Mortality</u>

The SUNSHINE study showed no statistically significant difference between treatment groups for the overall survival endpoint.

<u>Morbidity</u>

Global cure and cessation of diarrhoea

The global cure endpoint was defined as clinical response on or two days after the end of treatment manifested as the absence of watery diarrhoea (in patients < 2 years) or the nature of the bowel movements based on less than 3 unformed bowel movements (in patients > 2 years) on two consecutive days and stopping by the end of the study (30 days after the end of treatment) without evidence of disease recurrence.
In cases of recurrence of diarrhoea to a greater extent than that noted at the end of treatment, the stools were tested for toxigenic strains of *Clostridioides difficile*. Only disease courses of patients with a positive pathogen detection were defined as recurrent.

For the endpoint global cure, there is an effect modification by the characteristic sex. For boys there is a statistically significant disadvantage of fidaxomicin compared with vancomycin. For girls there, is no difference between the treatment groups. There are uncertainties regarding the clinical relevance of this sex-specific effect modification because of the low patient numbers in this sub-population as well as the results of the benefit assessment in adults. This effect modification is therefore not considered further in the present assessment.

For the endpoints global cure and cessation of diarrhoea, there are no clinically relevant differences between treatment arms for the relevant sub-population. In the summary of the results, there is no difference between fidaxomicin and vancomycin in the morbidity endpoint.

Quality of life

In the SUNSHINE study, endpoints in the endpoint category health-related quality of life were not investigated.

Side effects

For the endpoints serious adverse events (SAEs), discontinuation because of AEs, and the overall rates of adverse events, there was no statistically significant difference between fidaxomicin and vancomycin.

In the summary of the results there is no difference between fidaxomicin and vancomycin in the side effects category.

Overall assessment/conclusion

To assess the extent of the additional benefit of fidaxomicin, a sub-population of the single-blind, parallel, randomised, controlled SUNSHINE study was presented. Results on mortality, morbidity, and side effects are available. No health-related quality of life survey was carried out in the study.

For the overall survival endpoint, there was no statistically significant difference between fidaxomicin and vancomycin.

In the overall review of the results in the morbidity category for global cure and cessation of diarrhoea, there was no statistically significant difference between fidaxomicin and vancomycin.

In the overall view of the endpoints in the side effects category, for the endpoints serious adverse events (SAEs), discontinuation because of AEs, and the overall rates of adverse events, there was no statistically significant difference between fidaxomicin and vancomycin.

In summary, in the overall assessment of the results on mortality, morbidity, and side effects, there is no additional benefit of fidaxomicin compared with vancomycin for patients < 18 years of age with mild Clostridioides difficile-associated diarrhoea requiring treatment.

b) Patients < 18 years of age with severe and/or recurrent courses of Clostridioides difficile-associated diarrhoea

For patients < 18 years of age with severe and/or recurrent Clostridioides difficile-associated diarrhoea, there is a hint for a considerable additional benefit of fidaxomicin.

Justification:

Extent and probability of the additional benefit

Mortality

The SUNSHINE study showed no statistically significant difference between treatment groups for the overall survival endpoint.

Morbidity

Global cure and cessation of diarrhoea

The global cure endpoint was defined as clinical response on or two days after the end of treatment manifested as the absence of watery diarrhoea (in patients < 2 years) or the nature of the bowel movements based on less than 3 unformed bowel movements (in patients > 2 years) on two consecutive days and stopping by the end of the study (30 days after the end of treatment) without evidence of disease recurrence. In cases of recurrence of diarrhoea to a greater extent than that noted at the end of treatment, the stools were tested for toxigenic strains of Clostridioides difficile. Only disease courses of patients with a positive pathogen detection were defined as recurrent.

For the endpoint global cure, there was a statistically significant difference between treatment arms in favour of fidaxomicin for the relevant sub-population. This shows that in the treatment group with fidaxomicin, 72.5% of patients (37 out of 51) achieved a cure according to the above criteria; in the treatment group with vancomycin this was observed in only 38.7% of patients (12 out of 31). This advantage is classified as considerable.

For the endpoint “Cessation of diarrhoea”, there is no statistically significant difference between the treatment arms.

In the summary of the results on global cure and cessation of diarrhoea, there is a considerable additional benefit of fidaxomicin compared with vancomycin for the morbidity endpoint.

Quality of life

In the SUNSHINE study, endpoints in the endpoint category health-related quality of life were not investigated.

Side effects

For the endpoints serious adverse events (SAEs), discontinuation because of AEs, and the overall rates of adverse events, there was no statistically significant difference between fidaxomicin and vancomycin.

For the specific AEs, a statistically significant disadvantage of fidaxomicin compared with vancomycin was shown in the endpoint nervous system disorders (SOC). These events are all non-serious side effects that are not considered relevant for the assessment of the additional benefit.

In the category side effects, there were no clinically relevant differences between the treatment arms of the study in the overall view.

Overall assessment/conclusion

To assess the extent of the additional benefit of fidaxomicin, a sub-population of the single-blind, parallel, randomised, controlled SUNSHINE study was presented. Results on mortality,

morbidity, and side effects are available. No health-related quality of life survey was carried out in the study.

For the overall survival endpoint, there was no statistically significant difference between fidaxomicin and vancomycin.

In the overall review of the results in the morbidity category for global cure and cessation of diarrhoea, there is a considerable additional benefit of fidaxomicin compared with vancomycin because of the statistically significant difference in the global cure endpoint.
In the side effects category, for the endpoints serious adverse events (SAEs), discontinuation because of AEs, and the overall rates of adverse events, there are no clinically relevant differences between the treatment groups. At the level of individual specific AEs (nervous system disorders), a statistically significant difference to the detriment of fidaxomicin was determined. These events are all non-serious side effects that are not considered relevant for the assessment of the additional benefit.

Thus, an additional benefit of fidaxomicin compared with vancomycin is not proven for the endpoint side effects.

In summary, in the overall assessment of the results on mortality, morbidity, and side effects, there is a considerable additional benefit of fidaxomicin compared with vancomycin for patients < 18 years of age with severe and/or recurrent courses of Clostridioides difficile-associated diarrhoea.

Reliability of data (probability of additional benefit)

Because of the uncertainties in the distribution of patients by severity of the disease and the lack of blinding in the SUNSHINE study, there is only a hint for a considerable additional benefit.

2.1.4 Summary of the assessment

The present assessment refers to the benefit assessment of a new therapeutic indication for the active ingredient fidaxomicin. The therapeutic indication assessed here is as follows: Treatment of Clostridioides difficile infections (CDI) also known as Clostridioides difficile-associated diarrhoea (CDAD) in children and adolescents from birth up to an age of < 18 years. In the therapeutic indication to be considered, two patient groups were distinguished:

a) Patients < 18 years of age with mild courses of Clostridioides difficile-associated diarrhoea requiring treatment
b) Patients < 18 years of age with severe and/or recurrent courses of Clostridioides difficile-associated diarrhoea

a) Patients < 18 years of age with mild courses of Clostridioides difficile-associated diarrhoea requiring treatment

Metronidazole or vancomycin was determined as an appropriate comparator therapy by the G-BA.

For this group of patients, the pharmaceutical company presents a sub-population of the single-blind SUNSHINE RCT in which fidaxomicin was compared with vancomycin, thus implementing the appropriate comparator therapy.

In the categories mortality, morbidity, and side effects, there is no statistically significant difference between treatment groups. There was no survey of health-related quality of life.

Overall, there is no evidence of an additional benefit of fidaxomicin compared with vancomycin for children and adolescents < 18 years of age with mild disease courses of CDI requiring treatment.

b) Patients < 18 years of age with severe and/or recurrent courses of Clostridioides difficile-associated diarrhoea

Vancomycin was determined as an appropriate comparator therapy by the G-BA:

For this group of patients, the pharmaceutical company presents a sub-population of the single-blind SUNSHINE RCT in which fidaxomicin was compared with vancomycin, thus implementing the appropriate comparator therapy.

In the mortality category, there is no statistically significant difference between treatment groups. There was no survey of health-related quality of life.

For the endpoint global cure, there was a statistically significant difference between treatment arms in favour of fidaxomicin for the relevant sub-population. This shows that in the treatment group with fidaxomicin, 37 out of 51 patients achieved a cure according to the aforementioned criteria. In contrast, for only 12 of 31 patients in the vancomycin treatment group was a cure achieved. In the morbidity category for the global cure endpoint, fidaxomicin showed a considerable advantage compared with vancomycin. For the cessation of diarrhoea endpoint, there was no statistically significant difference.
In the side effects category, for the endpoints serious adverse events (SAEs), discontinuation because of AEs, and the overall rates of adverse events, there is no statistically significant difference between the treatment groups. However, in the specific endpoint nervous system disorders, there were statistically significant differences to the detriment of fidaxomicin. These events are all non-serious side effects that are not considered relevant for the assessment of the additional benefit.

There are uncertainties in the distribution of patients by severity of the disease and the lack of blinding in the SUNSHINE study.

Overall, for children and adolescents < 18 years of age with severe and/or recurrent CDI disease, there is a hint for a considerable additional benefit of fidaxomicin compared with vancomycin.

2.2 Number of patients or demarcation of patient groups eligible for treatment

The information on patient numbers is based on the target population in statutory health insurance (SHI).

The G-BA takes into account the patient numbers given in the dossier of the pharmaceutical company. However, these are subject to uncertainties because of the limited epidemiological data basis on incidence and prevalence in the present indication as well as the lack of information on projections and adjustments in the dossier. Overall, the patient numbers can be assumed to be underestimated.

2.3 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 Dificlir™ (active ingredient: fidaxomicin) at the following publicly accessible link (last access: 19 August 2020):

https://www.ema.europa.eu/documents/product-information/dificlir-epar-product-information_de.pdf

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 15 August 2020).

To facilitate comparability, the pharmaceutical costs were approximated both on the basis of the pharmacy sales price level and also the price less statutory rebates in accordance with Sections 130 and 130a SGB V. Based on consumption, the required number of packs according to potency was determined. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates.

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or co-morbidities) are not taken into account when calculating the annual treatment costs.

Treatment duration:

Designation of the therapy	Treatment mode	Number of treatments/patient/year	Treatment duration/treatment (days)	Treatment days/patient/ year
Medicinal product to be assessed				
Fidaxomicin	continuously, 2 × daily	10	1	10
Appropriate comparator therapy				
Patient population a)				
Metronidazole	continuously, 1 × daily	7	1	7
Vancomycin	continuously, 4 × daily	10	1	10
Patient population b)				
Vancomycin	continuously, 4 × daily	10	1	10

Usage and consumption:

The (daily) doses recommended in the product information or the marked publications were used as the basis for calculation.

If no maximum treatment duration is given in the product information, the treatment duration is calculated as the regular duration of the antibiotic therapy. The time unit “days” is used to calculate the “number of treatments/patient/year”, time between individual treatments, and for maximum treatment duration if specified in the product information. The annual treatment costs were calculated based on the assumption that a patient receives only one antibiotic therapy per year; further relapses are therefore not reflected in the annual treatment costs.

The recommended dose of metronidazole is given as a range in the respective product information. For better traceability, a mean dose of 1000 mg per day divided into two single doses was mapped for children and adolescents > 12 years of age.

The recommended daily dose of vancomycin varies according to the severity of the disease and is calculated at 500 mg per day for mild courses and 2000 mg per day for severe courses.

The average body measurements from the official representative statistics “Microcensus 2017 - body measurements of the population” were used to calculate the dosages as a function of the body weight (average body weight of 7.6 kg for children aged less than one year as well as 42.1 kg for children aged < 12 years).[2]

Because it is not always possible to achieve the exact calculated dose per day with the commercially available potencies, in these cases, the dose is rounded up or down to the next higher or lower available dose that can be achieved with the commercially available dosage strengths and the scalability of the pharmaceutical form concerned.

In the calculation, the shelf life of the medicinal products was taken into account, and any discard after expiry of the shelf life was included.

Designation of the therapy	Dosage/ application	Dose/patient/treatment days	Consumption by potency/treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Fidaxomicin	≥ 12.5 kg: 200 mg	400 mg	2 × 200 mg	10	20 × 200 mg
	7.0 – < 9.0 kg: 120 mg	240 mg	2 x 120 mg	10	20 × 120 mg
Appropriate comparator therapy					
Patient population a)					
Metronidazole	≥ 12 years: 500 mg	1 × 1000 mg	2 × 500 mg	7	14 × 500 mg
	< 1 year: 20–30 mg/kg =152–228 mg	152 – 228 mg	1 × 500 mg	7	7 × 500 mg
Vancomycin	≥ 12 years: 125 mg	500 mg	4 × 125 mg	10	40 × 125 mg
	< 1 year: 10 mg/kg = 76 mg	304 mg	0.6 × 500 mg	10	6 × 500 mg
Patient population b)					
Vancomycin	≥ 12 years: 2 × 250 mg	2000 mg	8 × 250 mg	10	80 × 250 mg
	< 1 year: 10 mg/kg = 76 mg	304 mg	0.6 × 500 mg	10	6 × 500 mg

[2] German Federal Office For Statistics, Wiesbaden 2018: http://www.gbe-bund.de

Costs:

Costs of the medicinal product:

Designation of the therapy	Package size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Fidaxomicin 200 mg	20 FCT	€ 1,795.11	€ 1.77	€ 101.89	€ 1,691.45
Fidaxomicin 40 mg/ml[3]	-	-	-	-	-
Appropriate comparator therapy					
Patient population a)					
Metronidazole 5 mg/ml[4]	10 IS	€ 69.15	€ 1.77	€ 4.74	€ 62.64
Metronidazole 500 mg[5]	20 FCT	€ 17.32	€ 1.77	€ 0.53	€ 15.02
Vancomycin 500 mg	10 TSS	€ 114.29	€ 1.77	€ 5.04	€ 107.48
Vancomycin 125 mg	28 HC	€ 261.81	€ 1.77	€ 43.61	€ 216.43
Patient population b)					
Vancomycin 500 mg	10 TSS	€ 114.29	€ 1.77	€ 5.04	€ 107.48
Vancomycin 250 mg	28 HC	€ 375.64	€ 1.77	€ 17.76	€ 356.11
FCT: film-coated tablets; HC: hard capsules; IS: infusion solution; DSS: dry substance without solvent					

Pharmaceutical retail price (LAUER-TAXE®) as last revised: 15 August 2020

Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be assessed and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed standard expenditure in the course of the treatment are not shown.

Because there are no regular differences in the necessary medical treatment or the prescription of other services when using the medicinal product to be assessed and the appropriate comparator therapy according to the product information, no costs for additionally required SHI services had to be taken into account.

[3] Fidaxomicin granulate 40 mg/ml is currently not available on the German market; a cost presentation is therefore not possible
[4] Fixed reimbursement rate
[5] Fixed reimbursement rate

3. Bureaucratic costs

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

At its session on 21 August 2018, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 11 March 2020, the pharmaceutical company submitted a dossier for the benefit assessment of fidaxomicin to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 2 VerfO.

By letter dated 11 March 2020 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient fidaxomicin.

The dossier assessment by the IQWiG was submitted to the G-BA on 10 June 2020, and the written statement procedure was initiated with publication on the website of the G-BA on 15 June 2020. The deadline for submitting written statements was 6 July 2020.

The oral hearing was held on 27 July 2020.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing were discussed at the session of the subcommittee on 25 August 2020, and the proposed resolution was approved.

At its session on 3 September 2020, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	21 August 2018	Determination of the appropriate comparator therapy
Working group Section 35a	15 July 2020	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	27 July 2020	Conduct of the oral hearing
Working group Section 35a	5 August 2020 19 August 2020	Consultation on the dossier assessment by the IQWiG, evaluation of the written statement procedure

Subcommittee on Medicinal Products	25 August 2020	Concluding discussion of the draft resolution
Plenum	3 September 2020	Adoption of the resolution on the amendment of Annex XII of the AM-RL

Berlin, 3 September 2020

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

Prof. Hecken