Gemeinsamer Bundesausschuss

Justification

of the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Dostarlimab (endometrial cancer, following prior treatment with a platinum-containing regimen)

of 2 December 2021

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 studies 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 benefits,
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 relevant date for the first placing on the (German) market of the combination of active ingredient dostarlimab in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO) is 15 June 2021. The pharmaceutical company submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM- NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 1 VerfO on 15 June 2021.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on the website of the G-BA (www.g-ba.de) on 15 September 2021, 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 dostarlimab 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, the statements submitted in the written statement and oral hearing procedure, and the addendum to the benefit assessment prepared by IQWiG. 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 dostarlimab.

In the light of the above and taking into account the statements received and the oral hearing, the G-BA has come to 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 dostarlimab (Jemperli) in accordance with the product information

Jemperli is indicated as monotherapy for the treatment of adult patients with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) recurrent or advanced endometrial cancer (EC) that has progressed on or following prior treatment with a platinum-containing regimen.

Therapeutic indication of the resolution (resolution from 2 December 2021):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adult patients with dMMR/MSI-H recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum-containing regimen

Appropriate comparator therapy:

Therapy according to doctor's instructions

[1] General Methods, version 6.0 from 05.11.2020. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

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.

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 products or non-medicinal treatments for which the Federal Joint Committee has already determined the patient-relevant benefit 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 addition to dostarlimab, the following active ingredients are approved for the present therapeutic indication: cisplatin, doxorubicin, medroxyprogesterone acetate and megestrol acetate.

on 2. A non-medicinal treatment does not come into question for the present therapeutic indication.

on 3. No corresponding resolutions or assessments of the G-BA are available.

on 4. The general state of medical knowledge in the present therapeutic indication was represented by a systematic search for guidelines and reviews of clinical studies.

According to the present state of knowledge, there are no specific therapy recommendations depending on the MSI-H/dMMR status.

Furthermore, the available evidence does not indicate the association of MSI-H/dMMR endometrial cancer with specific factors that clearly argue against treatment with the previous or current standard therapies. Thus, those therapy options that are independent of the MSI-H/dMMR status and thus, eligible for the unselected patient population in this respect are considered for the appropriate comparator therapy.

The available evidence indicates, among others, systemic chemotherapy, which can also be a platinum-containing re-therapy for the present treatment situation. According to the authorisation status, the active ingredients cisplatin and doxorubicin can be considered for this purpose. In addition, the guidelines recommend chemotherapy with carboplatin in combination with paclitaxel. In addition, according to the statement of the scientific-medical societies, monotherapy with paclitaxel represents a relevant treatment option in the therapeutic indication.

The active ingredients carboplatin and paclitaxel are not approved for the present indication. There is a discrepancy between medicinal products approved in the indication and those used in health care/recommended by the guidelines.

Furthermore, according to guidelines and statements of the scientific-medical societies, endocrine therapy can be considered as a treatment option for the present treatment situation.

Taking into account the advanced stage of the disease and treatment, the G-BA also considers best supportive care to be a treatment option.

Overall, the G-BA determines a therapy according to the doctor’s instructions as an appropriate comparator therapy on the basis of the underlying evidence.

As part of the therapy according to the doctor's instructions, endocrine therapy with the active ingredients medroxyprogesterone acetate, megestrol acetate as well as systemic chemotherapy, which can also be platinum-containing re-therapy, with cisplatin (monotherapy or in combination with doxorubicin), doxorubicin (monotherapy or in combination with cisplatin), paclitaxel (monotherapy) as well as carboplatin in combination paclitaxel and best supportive care alone are considered eligible comparators.

Best Supportive Care (BSC) is understood as the therapy that ensures the best possible, patient-individually optimised, supportive treatment to alleviate symptoms and improve quality of life.

For the implementation of the therapy according to the doctor’s instructions, the comparison for the benefit assessment should include several of the above-mentioned treatment options and adequately represent the therapies frequently used in the reality of care in Germany. The choice of comparators used must be justified in the dossier for the benefit assessment. Considering the number of treatment options available in the context of therapy according to the doctor’s instructions, a single-comparator comparison does not appear to be appropriate. However, this procedure would have to be justified separately should only a single-comparator comparison be carried out.

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

Change of the appropriate comparator therapy

As part of the therapy according to the doctor's instructions, monotherapy with paclitaxel is added as a further eligible comparator.

However, irrespective of the question of the sufficient implementation of the appropriate comparator therapy, the data submitted by the pharmaceutical company were not suitable to prove an additional benefit, which is why the change of the appropriate comparator therapy does not require repetition of the benefit assessment procedure.

2.1.3 Extent and probability of the additional benefit

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

Adult patients with dMMR/MSI-H recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum-containing regimen

An additional benefit is not proven.

Justification:

Data basis:

In the dossier for the benefit assessment, the pharmaceutical company submits the results of the marketing authorisation study on dostarlimab. This is the GARNET study, which included patients with recurrent or advanced endometrial cancer with progressive disease on or following treatment with a platinum-containing doublet chemotherapy.

GARNET

The GARNET study is a single-arm, ongoing phase I study. Depending on the mismatch repair (MMR)/microsatellite (MS) status, these patients were divided into two cohorts (cohort A1: dMMR/MSI-H, cohort A2: MMR competence/microsatellite stability (MSS)).

Primary endpoints of the study are endpoints in the category of side effects as well as the endpoints of objective response rate and duration of response.

Patient-relevant secondary endpoints are assessed in the categories of overall survival, morbidity and health-related quality of life.

The study is being conducted in 123 study centres across Europe and North America.

Comparison data

The GARNET marketing authorisation study is an uncontrolled study. Thus, this study does not include a comparison group which allows comparison of the results of treatment with dostarlimab.

For a comparison of dostarlimab, the pharmaceutical company identified the RCTs, ZoptEC and IXAMPLE2 and the retrospective single-arm studies, Julius et al. (2013), Makker et al. (2013), Mazgani et al. (2008), and Rubinstein et al. (2019).

In addition, the pharmaceutical company presents data from the English registry study 216960.

In the dossier, the pharmaceutical company compares the results of cohort A1 (dMMR/ MSI-H) from the GARNET study with the results of individual arms from the aforementioned comparison studies on the appropriate comparator therapy. Depending on data availability (individual patient data (IPD) or aggregated data), indirect comparisons, based on an Inverse Probability of Treatment Weighting (IPTW) analysis (ZoptEC study) or on a Matching Adjusted Indirect Comparison (MAIC) analysis (further studies), are used by the pharmaceutical company. In its written statement, the pharmaceutical company also provides an IPTW analysis for the indirect comparison of the GARNET study with the registry study 216960.

ZoptEC

The ZoptEC study is a completed, randomised, controlled, open-label phase III study, comparing doxorubicin to zoptarelin. The pharmaceutical company uses the doxorubicin arm for comparison with dostarlimab.

Registry study 216960

Registry study 216960 is a retrospective study, conducted by the pharmaceutical company in collaboration with Health Data Insight (HDI), using data available through the National Cancer Registration and Analysis Service (NCRAS). The objective of the pharmaceutical company's study was to evaluate patient characteristics, treatment pathways and patterns of disease progression in patients with recurrent or advanced endometrial cancer in England from 2013 to 2018.

Assessment:

For the benefit assessment, the pharmaceutical company submitted the results of the GARNET marketing authorisation study.

The results from the GARNET study alone are not suitable for assessing the additional benefit of dostarlimab as they do not allow a comparison with the appropriate comparator therapy.

The pharmaceutical company compares the results of cohort A1 (dMMR/ MSI-H) from the GARNET study with the results of individual arms from the aforementioned studies on the appropriate comparator therapy.

MSI-H/ dMMR tumour status

Dostarlimab is approved for patients with recurrent or advanced endometrial cancer following prior platinum-based therapy whose tumour has a dMMR or MSI-H. Accordingly, the pharmaceutical company only considers cohort A1 from the GARNET study, which included patients with dMMR/ MSI-H.

In the context of the studies on the appropriate comparator therapy, the pharmaceutical company does not submit any information on the existence of the MSI-H/ dMMR status.

Regarding the question on the extent to which the MSI-H/dMMR status is a relevant prognostic factor, which underlies the assumption of sufficient similarity of the populations, the present benefit assessment procedure - the information in the pharmaceutical company's dossier, IQWiG's dossier assessment and the statements of the scientific-medical societies on this question - gives a heterogeneous and thus, inconclusive picture.

Therefore, the significance of the MSI-H/ dMMR tumour status cannot be conclusively assessed according to the present state of medical knowledge.

Methodology of the comparison of individual arms of different studies

Apart from the data of the registry study 216960 and the ZoptEC study, the pharmaceutical company only presents aggregated data on the studies on the appropriate comparator therapy. Each one of the indirect comparisons with the GARNET study presented by the pharmaceutical company for these studies is based on MAIC analyses without a bridge comparator.

MAIC analyses without a bridge comparator are generally not an adequate way to adjust for confounders. In the case of non-randomised comparisons without a bridge comparator, only those procedures that are carried out using IPD, in contrast to MAIC analysis, are generally useful for confounder adjustment. In contrast, the MAIC analysis accounts for confounding based on aggregate data. Thus, all comparisons performed by the pharmaceutical company on the basis of MAIC analyses without a bridge comparator are not suitable for the assessment of the additional benefit of dostarlimab. In light of this, the IXAMPLE2, Julius et al. (2013), Makker et al. (2013), Mazgani et al. (2008) and Rubinstein et al. (2019) studies are not used for the benefit assessment.

Confounder adjustment - indirect comparisons GARNET versus ZoptEC or registry study 216960

The pharmaceutical company adequately identified the potential confounders for the comparison of the individual arms from the relevant studies.

However, for neither of the two comparisons of individual arms does the pharmaceutical company present an analysis that takes into account all the confounders classified as relevant.

Following the confounder adjustment, an approximation of the adjusted characteristics is achieved to a large extent, but relevant differences remain between the groups with regard to the unadjusted characteristics as the confounders are not taken into account.

Thus, in both indirect comparisons submitted by the pharmaceutical company, no sufficient structural equality of the treatment groups can be achieved by the adjustment made.

Overall, the confounder adjustment performed by the pharmaceutical company for the comparison of the dostarlimab arm of the GARNET study with the doxorubicin arm of the ZoptEC study or with the comparator arm from the registry study 216960 is assessed as inadequate.

In light of this, the results of the adjusted analysis of the indirect comparisons of the GARNET study versus the ZoptEC or registry study 216960 are not significant and are not used for the benefit assessment.

<u>Conclusion:</u>

Overall, the data presented are unsuitable to demonstrate an additional benefit compared to the appropriate comparator therapy, which is why an additional benefit of dostarlimab as monotherapy in adult patients with dMMR/ MSI-H recurrent or advanced endometrial cancer, who show disease progression on or following prior platinum-containing regimen, is not proven.

Dostarlimab may represent a relevant treatment option in the present therapeutic indication.

2.1.4 Summary of the assessment

The benefit assessment is carried out for the new medicinal product Jemperli with the active ingredient dostarlimab.

This medicinal product was approved under special conditions.

Jemperli is indicated as monotherapy for the treatment of adult patients with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) recurrent or advanced endometrial cancer (EC) that has progressed on or following prior treatment with a platinum-containing regimen..

The G-BA determined the appropriate comparator therapy to be a therapy according to the doctor's instructions that may include endocrine therapy, chemotherapy and best supportive care.

For the benefit assessment, the pharmaceutical company submitted the results from the GARNET marketing authorisation study for the treatment with dostarlimab. This is an uncontrolled study and therefore, does not include a comparison group.

For a comparison with the appropriate comparator therapy, the pharmaceutical company presents adjusted indirect comparisons of the results of cohort A1 (dMMR/ MSI-H) from the GARNET study versus the results of individual arms from the ZoptEC and 216960 registry studies.

Overall, the data presented are unsuitable to demonstrate an additional benefit compared to the appropriate comparator therapy, which is why an additional benefit of dostarlimab as monotherapy in adult patients with dMMR/ MSI-H recurrent or advanced endometrial cancer, who show disease progression on or following prior platinum-containing regimen, is not proven.

Dostarlimab may represent a relevant treatment option in the present therapeutic indication.

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

The information on the number of patients is based on the target population in statutory health insurance (SHI).

The resolution is based on the information from the dossier of the pharmaceutical company regarding the number of patients as well as the information of an assessment expert.

Both the number of 613 to 3,358 patients stated by the pharmaceutical company and the number of 226 to 732 patients in the SHI target population stated by the assessment expert are subject to uncertainty.

Overall, uncertainty is to be assumed due to the contrary deviations in the pharmaceutical company's estimate with regard to the baseline. Furthermore, the application of proportionate values from the incidence base to the 5-year prevalence and the partly unclear

transferability of the proportionate values due to different patient collectives in the data sources used lead to uncertainties.

According to the assessment expert's information, there are uncertainties due to the restriction to an incidence-based approach, the lack of limitation to patients with the diagnosis code C54.1 and the lack of consideration of advanced endometrial cancer.

Based on the data presented, a number of 226 to 3,358 patients in the SHI target population formed over both ranges can be estimated.

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 Jemperli (active ingredient: dostarlimab) at the following publicly accessible link (last access: 8 November 2021):

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

Treatment with dostarlimab should only be initiated and monitored by specialists in internal medicine, haematology and oncology, specialists in obstetrics and gynaecology, and specialists participating in the Oncology Agreement who are experienced in the treatment of patients with endometrial cancer.

This medicinal product was approved under "special conditions". This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

All doctors prescribing JEMPERLI must inform patients about the patient card and explain what to do in case of symptoms of immune-mediated side effects. The doctor provides each patient with a patient card.

The dMMR/MSI-H tumour status should be determined using a validated investigation method.

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 November 2021).

Treatment period:

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration is patient-individual and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

The annual treatment costs shown refer to the first year of treatment.

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Dostarlimab	Cycle 1-4: 1 x per 21 day cycle	4	1	4
Dostarlimab	Afterwards: 1 x per 42 day cycle	6.7	1	6.7
Best supportive care	Different from patient to patient			

Appropriate comparator therapy				
Therapy according to doctor's instructions[a]				
Medroxyprogesterone acetate	1 - 3 x daily	365	1	365
Megestrol acetate	1 x daily	365	1	365
Cisplatin monotherapy				
Cisplatin	1 x per 21 day cycle	17.4	1	17.4
	or			
	1 x per 28 day cycle	13	1	13
	or			
	on day 1 - 5, 21-day cycle	17.4	5	87
	or			
	on day 1 - 5, 28-day cycle	13	5	65
Doxorubicin monotherapy				
Doxorubicin	1 x per 21 day cycle	17.4	1	17.4
Cisplatin + doxorubicin[2]				
Cisplatin	1 x per 21 day cycle	6	1	6
Doxorubicin	1 x per 21 day cycle	6	1	6
Best supportive care		Different from patient to patient		
[a] The active ingredients carboplatin and paclitaxel are suitable comparators for the present benefit assessment in the context of therapy according to doctor's instructions. However, these medicinal products are not approved in the present therapeutic indication, and therefore, no costs are presented for these medicinal products.				

Consumption:

The product information on medroxyprogesterone acetate specifies the most common dosage of 300 - 600 mg per day for the treatment of endometrial cancer. A dosage of 250 mg - 500 mg is presented for the present calculation.

[2] Nomura H et al.: Japanese Gynaecologic Oncology Group. Effect of Taxane Plus Platinum Regimens vs Doxorubicin Plus Cisplatin as Adjuvant Chemotherapy for Endometrial Cancer at a High Risk of Progression: A Randomised Clinical Trial. JAMA Oncol. 2019 Jun 1;5(6):833-840. doi: 10.1001/jamaoncol.2019.0001.

The study by Nomura et al. (2019)[2] is used to calculate the dosage of the combination therapy of cisplatin and doxorubicin.

The average body measurements of adult females were applied for dosages, depending on body weight (BW) or body surface area (BSA)(average body height: 1.66 m; average body weight: 68.7 kg). This results in a body surface area of 1.76 m² (calculated according to Du Bois 1916).

Designation of the therapy	Dosage/ application	Dosage/ patient/ treatment days	Usage by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Dostarlimab	Cycle 1-4: 500 mg Afterwards: 1,000 mg	500 mg 1,000 mg	1 x 500 mg 2 x 500 mg	4 6.7	4 x 500 mg 13.4 x 500 mg
Best supportive care		Different from patient to patient			
Appropriate comparator therapy					
- Therapy according to doctor's instructions[a]					
Medroxyprogesterone acetate	125 mg -	300 mg -	1 x 250 mg	365	365 x 250 mg -
	250 mg	600 mg	1 x 500 mg		365 x 500 mg
Megestrol acetate	80 mg -	80 mg -	0.5 x 160 mg	365	182.5 x 160 mg
	320 mg	320 mg	2 x 160 mg		730 x 160 mg
Cisplatin monotherapy					
Cisplatin	50 mg/m² body surface area = 88 mg	88 mg	2 x 50 mg	17.4	34.8 x 50 mg
	or				
	120 mg/m² body surface area = 211.20 mg	211.20 mg	5 x 50 mg	13	65 x 50 mg
	or				
	15 mg/m² body surface area = 26.4 mg	26.4 mg	1 x 50 mg	87	87 x 50 mg
	or				

Designation of the therapy	Dosage/ application	Dosage/ patient/ treatment days	Usage by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	20 mg/m² body surface area = 35.2 mg	35.2 mg	1 x 50 mg	65	65 x 50 mg
Doxorubicin monotherapy					
Doxorubicin	60 mg/m² = 105.6 mg	105.6 mg -	1 x 100 mg + 1 x 10 mg -	17.4	17.4 x 100 mg + 17.4 x 10 mg
	75 mg/m² = 132 mg	132 mg	1 x 150 mg	17.4	17.4 x 150 mg
Cisplatin + doxorubicin[2]					
Cisplatin	50 mg/m² body surface area = 88 mg -	88 mg	2 x 50 mg -	6	12 x 50 mg -
Doxorubicin	60 mg/m² = 105.6 mg	105.6 mg	1 x 100 mg + 1 x 10 mg	6	6 x 100 mg + 6 x 10 mg
Best supportive care		Different from patient to patient			
[a] The active ingredients carboplatin and paclitaxel are suitable comparators for the present benefit assessment in the context of therapy according to doctor's instructions. However, these medicinal products are not approved in the present therapeutic indication, and therefore, no costs are presented for these medicinal products.					

Costs:

Costs of the medicinal products:

Designation of the therapy	Packaging 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					
Dostarlimab 500 mg	1 CIS	€ 5,930.32	€ 1.77	€ 338.10	€ 5,590.45
Best supportive care	Different from patient to patient				

Appropriate comparator therapy					
Medroxyprogesterone acetate 250 mg	50 TAB	€ 104.57	€ 1.77	€ 5.18	€ 97.62
Medroxyprogesterone acetate 500 mg	100 TAB	€ 355.49	€ 1.77	€ 19.07	€ 334.65
Megestrol acetate 160 mg	30 TAB	€ 493.96	€ 1.77	€ 26.74	€ 465.45
Cisplatin 50 mg	1 CIS	€ 47.46	€ 1.77	€ 1.73	€ 43.96
Doxorubicin 100 mg[3]	1 CIS	€ 285.52	€ 1.77	€ 0.00	€ 283.75
Doxorubicin 10 mg[3]	1 CIS	€ 40.04	€ 1.77	€ 2.29	€ 35.98
Doxorubicin 150 mg[3]	1 SFI	€ 418.08	€ 1.77	€ 0.00	€ 416.31
Best supportive care	Different from patient to patient				
Abbreviations: CIS = concentrate for the preparation of an infusion solution; SFI = solution for injection; TAB = tablets					

LAUER-TAXE® last revised: 15 November 2021

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 evaluated 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.

Non-prescription medicinal products that are reimbursable at the expense of the statutory health insurance according to Annex I of the Pharmaceuticals Directive (so-called OTC exception list) are not subject to the current medicinal products price regulation. Instead, in accordance with Section 129 paragraph 5aSGB V, when a non-prescription medicinal product is dispensed and invoiced in accordance with Section 300, a medicinal product dispensing price in the amount of the dispensing price of the pharmaceutical company plus the surcharges in accordance with Sections 2 and 3 of the Pharmaceutical Price Ordinance in the version valid on 31 December 2003 applies to the insured.

[3] Fixed reimbursement rate

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Treatment days/ year	Costs/ patient/ year
Appropriate comparator therapy							
Cisplatin							
In clinical practice, an appropriate antiemetic treatment is established before and/or after administration of cisplatin. The product information for cisplatin does not provide any specific information on this, which is why the necessary costs cannot be quantified.							
17.4 cycles:							
Mannitol 10% infusion solution, 37.5 g/day	10 x 500 ml INF	€ 106.22	€ 5.31	€ 9.81	€ 91.10	17.4	€ 158.51
Sodium chloride 0.9% infusion solution, 3 - 4.4 l/day	10 x 1,000 ml INF	€ 35.47	€ 1.77	€ 1.12	€ 32.58	17.4	€ 170.07 - € 263.11
	10 x 500 ml INF	€ 22.72	€ 1.14	€ 0.69	€ 20.89		
13 cycles:							
Mannitol 10% infusion solution, 37.5 g/day	10 x 500 ml INF	€ 106.22	€ 5.31	€ 9.81	€ 91.10	13	€ 118.43
Sodium chloride 0.9% infusion solution, 3 - 4.4 l/day	10 x 1,000 ml INF	€ 35.47	€ 1.77	€ 1.12	€ 32.58	13	€ 127.06 - € 196.57
	10 x 500 ml INF	€ 22.72	€ 1.14	€ 0.69	€ 20.89		
6 cycles:							
Mannitol 10% infusion solution, 37.5 g/day	10 x 500 ml INF	€ 106.22	€ 5.31	€ 9.81	€ 91.10	6	€ 91.10
Sodium chloride 0.9% infusion solution, 3 - 4.4 l/day	10 x 1,000 ml INF	€ 35.47	€ 1.77	€ 1.12	€ 32.58	6	€ 65.16 - 97.74
Abbreviations: CIS = concentrate for the preparation of an infusion solution; SFI = solution for injection; INF = infusion solution; TAB = tablets							

Other SHI services:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe) (Sections 4 and 5 of the Pharmaceutical Price Ordinance) from 01.10.2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131 paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic agents a maximum of € 81 per ready-to-use preparation and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 71 per ready-to-use unit are to be payable. These additional other costs are not added to the pharmacy sales price but follow the rules for calculating in the Hilfstaxe. The cost representation is based on the pharmacy sales price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

3. Bureaucratic costs calculation

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 26 May 2020, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 15 June 2021, the pharmaceutical company submitted a dossier for the benefit assessment of dostarlimab to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 16 June 2021 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 dostarlimab.

The dossier assessment by the IQWiG was submitted to the G-BA on 13 September 2021, and the written statement procedure was initiated with publication on the website of the G-BA on 15 September 2021. The deadline for submitting written statements was 6 October 2021.

The oral hearing was held on 25 October 2021.

By letter dated 26 October 2021, the IQWiG was commissioned with supplementary assessments of data submitted in the written statement procedure. The addenda prepared by IQWiG was submitted to the G-BA on 12 November 2021.

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 23 November 2021, and the proposed resolution was approved.

At its session on 2 December 2021, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal product	26 May 2020	Determination of the appropriate comparator therapy
Working group Section 35a	20 October 2021	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal product	25 October 2021	Conduct of the oral hearing, Commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	3 November 2021 17 November 2021	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Subcommittee Medicinal product	23 November 2021	Concluding discussion of the draft resolution
Plenum	2 December 2021	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 2 December 2021

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

Prof. Hecken