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 Polatuzumab Vedotin (Diffuse Large B-Cell Lymphoma, Combination with Bendamustine and Rituximab)

of 20 August 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.

For medicinal products for the treatment of a rare disease (orphan drugs) that are approved according to Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999, the additional medical benefit is considered to be proven through the grant of the marketing authorisation according to Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V. Evidence of the medical benefit and the additional medical benefit in relation to the appropriate comparator therapy need not be submitted (Section 35a, paragraph 1, sentence 11, 2nd half of the sentence SGB V). Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V thus guarantees an additional benefit for an approved orphan drug, although an assessment of the orphan drug in accordance with the principles laid down in Section 35a, paragraph 1, sentence 3, Nos. 2 and 3 SGB V in conjunction with Chapter 5, Sections 5 et seq. of the Rules of Procedure (VerfO) of the G-BA has not been carried out. In accordance with Section 5, paragraph 8 AM-NutzenV, only the extent of the additional benefit is to be quantified indicating the significance of the evidence.

However, the restrictions on the benefit assessment of orphan drugs resulting from the statutory obligation to the marketing authorisation do not apply if the turnover of the medicinal product with the SHI at pharmacy sales prices and outside the scope of SHI-accredited medical care, including VAT, exceeds € 50 million during the last twelve calendar months. According to Section 35a, paragraph 1, sentence 12 SGB V, the pharmaceutical company must then, within three months of being requested to do so by the G-BA, submit evidence according to Chapter 5, Section 5, paragraphs 1–6 VerfO, in particular regarding the additional medicinal benefit in relation to the appropriate comparator therapy as defined by the G-BA according to Chapter 5, Section 6 VerfO and prove the additional benefit in comparison with the appropriate comparator therapy.

In accordance with Section 35a, paragraph 2 SGB V, the G-BA decides whether to carry out the benefit assessment itself or to commission the Institute for Quality and Efficiency in Health Care (IQWiG). On the basis of the statutory requirement in Section 35a, paragraph 1, sentence 11 SGB V that the additional benefit of an orphan drug is deemed to have been proven through the grant of marketing authorisation, the G-BA modified the procedure for the benefit assessment of orphan drugs at its session on 15 March 2012 to the effect that, in the case of orphan drugs, the G-BA initially no longer independently determines an appropriate comparator therapy as the basis for the solely legally permissible assessment of the extent of an additional benefit to be assumed by law. Rather, the extent of the additional benefit provided is assessed exclusively on the basis of the approval studies by the G-BA indicating the significance of the evidence.

Accordingly, at its session on 15 March 2012, the G-BA amended the mandate issued to the IQWiG by resolution of 1 August 2011 for the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a, paragraph 2 SGB V to that effect that, in the case of orphan drugs, the IQWiG is only commissioned to carry out a benefit assessment in the case of a previously defined comparator therapy when the sales volume of the medicinal product concerned has exceeded the legal limit of € 50 million and is therefore subject to an unrestricted benefit assessment (*cf* Section 35a, paragraph 1, sentence 12 SGB V). According to Section 35a, paragraph 2 SGB V, the assessment of the G-BA 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 market of the active ingredient polatuzumab vedotin in accordance with Chapter 5, Section 8, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO) is 15 February 2020. 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, number 1 VerfO on 22 January 2020.

Polatuzumab vedotin for the treatment of adult patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) is approved as a medicinal product for the treatment of a rare disease under Regulation (EC) No 141/2000 of the European Parliament and the Council of 16 December 1999.

In accordance with Section 35a, paragraph 1, sentence 11, 1st half sentence SGB V, the additional benefit is considered to be proven through the grant of the marketing authorisation. The extent of the additional benefit and the significance of the evidence are assessed by the G-BA on the basis of the approval studies.

The G-BA carried out the benefit assessment and commissioned the IQWiG to evaluate the information provided by the pharmaceutical company in Module 3 of the dossier on treatment costs and patient numbers. The benefit assessment was published on 15 May 2020 together with the IQWiG assessment 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 has adopted its resolution on the basis of the dossier of the pharmaceutical company, the dossier assessment carried out by the G-BA, the assessment of treatment costs and patient numbers (IQWiG G12-01) 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 evaluated the studies relevant for marketing authorisation with regard to their therapeutic relevance (qualitative) in accordance with the criteria laid down in Chapter 5, Section 5, paragraph 7, sentence 1, numbers 1 through 4 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of polatuzumab vedotin.

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

2.1.1 Approved therapeutic indication of polatuzumab vedotin (Polivy®) in accordance with the product information

Polivy in combination with bendamustine and rituximab is indicated for the treatment of adult patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) who are not candidates for haematopoietic stem cell transplant.

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.

2.1.2 Extent of the additional benefit and the significance of the proof

Adult patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) who are not candidates for haematopoietic stem cell transplant

In summary, the additional benefit of polatuzumab vedotin in combination with bendamustine and rituximab is assessed as follows:

Hint for a non-quantifiable additional benefit because the scientific data does not permit quantification.

Justification:

The pharmaceutical company presented data from the pivotal, multi-centre, multi-arm, open-label Phase Ib/II GO29365 study for the benefit assessment. In the randomised, controlled part of Phase II of the study, treatment with polatuzumab vedotin in combination with bendamustine and rituximab or bendamustine in combination with rituximab was investigated in Arms A and B in patients with relapsed or refractory (r/r) follicular lymphoma (FL) and in Arms C and D in patients with r/r diffuse large cell B-cell lymphoma (DLBCL). The non-comparative expansion part of Phase II of the study investigated polatuzumab vedotin in combination with bendamustine and obinutuzumab in patients with r/r FL (Arm E) and r/r DLBCL (Arm F) as well as in combination with bendamustine and rituximab in patients with r/r DLBCL (Arms G and H).

For the present assessment, the randomised, controlled comparison of arm C (hereinafter intervention arm: polatuzumab vedotin in combination with bendamustine and rituximab) with arm D (hereinafter comparison arm: bendamustine in combination with rituximab) is used.

The two relevant study arms included adult patients with EGOC-PS ≤ 2 and histologically confirmed DLBCL. The patients had to have received at least one prior therapy for DLBCL to which they were refractory or developed a relapse. Furthermore, they should not have been eligible for haematopoietic stem cell transplant (HSCT). Reasons for ineligibility for HSCT were age, previous transplant failure, or an inadequate response to salvage therapy (intervention arm vs comparison arm each: 32.5% vs 47.5%; 25% vs 15%; 30% vs 22.5%). In both study arms, patients had received two prior anti-lymphoma therapies (median). Patients with HIV infection were excluded from the GO29365 study.

In both the intervention arm and the comparator arm, 40 patients each were randomised and stratified by to the duration of response to the last previous therapy (≤ 12 months vs > 12 months).

Patients were to be treated for six cycles of 21 days each provided that none of the termination criteria (disease progression, the occurrence of unacceptable side effects, pregnancy, dose delay ≥ 4 weeks, or hepatitis B reactivation) had occurred earlier.

The primary endpoint for the randomised controlled comparison was complete response. Other endpoints include overall survival, symptomatology, and adverse events. Data on health-related quality of life were not collected in the GO29365 study.

For all endpoints except the complete response, the present assessment is based on the results of the data cut-off of 2 January 2020 submitted by the pharmaceutical company with the written statement. This data cut-off was created according to statements of the pharmaceutical company in order to comply with the requirements of the EMA. For the endpoint complete response, the results of the data cut-off of 30 April 2018 are used.

Mortality

In the GO29365 study, overall survival is defined as the time from randomisation to death of any cause.

As of the data cut-off of 2 January 2020, 26 patients in the intervention arm (65.0%) and 29 in the comparator arm (72.5%) had died. The median survival time in the intervention arm is 12.4 months compared with 4.7 months in the comparator arm. The median follow-up for both study arms was approx. 42 months. This corresponds to a median prolongation of 7.7 months. In the time-to-event analysis, a statistically significant difference is shown for the duration of the response to the last therapy (≤ 12 v. > 12 months) (hazard ratio (HR): 0.42; 95% confidence interval (CI): [0.24; 0.73]; p value = 0.0014) to the advantage of polatuzumab vedotin in combination with bendamustine and rituximab.

For overall survival, there was a significant benefit of treatment with polatuzumab vedotin in combination with bendamustine and rituximab.

Morbidity

Complete response (CR)

In the GO 29365 study, the endpoint complete response (CR) was defined as the frequency of patients achieving a complete response at the time of the primary response assessment (6–8 weeks after Day 1 of Cycle 6 or the last administration of the study medication).

A complete response (CR) was found in 16 patients (40%) of the intervention arm and seven patients (17.5%) of the comparator arm. The difference is statistically significant in favour of polatuzumab vedotin in combination with bendamustine and rituximab.

The complete response (CR) endpoint is an important prognostic factor and relevant for therapeutic decision-making. A CR associated with a noticeable decrease in disease symptoms for the patient is always relevant to patients for the benefit assessment. In the GO29365 study, the endpoint CR was assessed by imaging techniques using the modified Lugano criteria. Thus, the endpoint was assessed not on the basis of symptoms but rather on asymptomatic findings. Valid data on disease-related symptomatology are not available from the GO29365 study.

There is no validation of CR as a surrogate parameter for patient-relevant endpoints (e.g. mortality). For this reason, CR is classified as an endpoint of unclear relevance in the present assessment and is only presented additionally. No statement can be derived on the extent of the additional benefit.

Symptomatology

In the GO29365 study, the symptomatology of the patients assessed using the neuropathy-specific TINAS (Therapy-Induced Neuropathy Assessment Scale) questionnaire v1.0. Because the validity of this measuring instrument could not be proven by the pharmaceutical company, the results are not used for the present assessment.

Overall, the results of the GO29365 study do not allow a statement to be made on the extent of the additional benefit in terms of morbidity.

Quality of life

The GO29365 study did not survey data on health-related quality of life. Based on the GO29365 study, no statement can be made about the extent of the additional benefit in terms of quality of life.

Side effects

Adverse events (AE) in total

Almost all patients in the intervention and comparator arm experienced an adverse event. The results for the endpoint “total adverse events” are presented additionally.

Serious AE

In the GO 29365 study, approx. 67% of patients in the intervention arm and approx. 62% of patients in the comparator arm experienced a serious adverse event (SAE). The time-to-event analysis shows no statistically significant difference.

Severe AE (CTCAE grade ≥ 3)

A severe adverse event (CTCAE grade ≥ 3) was experienced by approx. 87% of patients in the intervention arm and approx. 74% of patients in the comparator arm. The time-to-event analysis shows no statistically significant difference.

Therapy discontinuation because of AE

Approx. 33% of patients in the intervention and 13% in the comparator arm discontinued treatment because of adverse events.

The time-to-event analysis shows a statistically significant difference to the disadvantage of polatuzumab vedotin in combination with bendamustine and rituximab (HR of 2.79; 95% CI: 0.98; 7.89; p value: 0.0442).

AE of special interest

In detail, only for “Peripheral neuropathy” and “Cardiac toxicity and arrhythmias” are there statistically significant differences between the treatment arms for the AE of special interest. There is both an advantage (cardiac toxicity and arrhythmias) and disadvantage (peripheral neuropathy) of polatuzumab vedotin in combination with bendamustine and rituximab.

In the assessment of the endpoints on side effects, in the present case, it is taken into account for the endpoint therapy discontinuation because of AE that the confidence interval for the effect estimator HR encompasses the value 1 if the p value is significant. Secondly, that discontinuation of therapy for reasons other than AE is a competing event for the endpoint therapy discontinuation because of AE. Such a competing event can be, for example, disease progression. In the present case, this occurred significantly more frequently in the comparator arm. Patients who had already discontinues therapy because of disease progression cannot stop again because of an AE. In the study documents, there is no information about a priori defined competing events or the use of computing risk models to address this problem. The influence of competing events on the results of the endpoint can therefore not be assessed conclusively.

In the overall view of the endpoints on side effects, because of its potentially strong bias, the result on the endpoint therapy discontinuation because of AE is not considered sufficient to derive an overall disadvantage for polatuzumab vedotin in combination with bendamustine and rituximab with the required certainty in the endpoint category side effects.

<u>Overall assessment</u>

For the benefit assessment of polatuzumab vedotin in combination with bendamustine and rituximab for the treatment of adult patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) who are not candidates for haematopoietic stem cell transplant, results on overall survival, morbidity, and side effects of the combination of bendamustine and rituximab from the GO29365 study are available. From the multi-arm study, the randomised controlled comparison of the study arms C (intervention arm) and D (comparison arm) is used for the assessment.

In the endpoint category mortality, there is a statistically significant difference to the advantage of polatuzumab vedotin in combination with bendamustine and rituximab. Compared with treatment with bendamustine in combination with rituximab, there is a significant advantage.

No conclusions on the extent of the additional benefit can be drawn from the results on the morbidity endpoint complete response. With regard to the symptomatology, the results of the neuropathy-specific TINAS questionnaire cannot be used because of its lack of validity.

In the study, no data on health-related quality of life were collected. Therefore, no statement can be made about the extent of the additional benefit in terms of quality of life.

The results on side effects do not show any differences relevant to the assessment.

The overall assessment of the extent of the additional benefit takes into account that the results of the GO29365 study are subject to significant uncertainties and limitations. One uncertainty of the GO29365 study is the small sample size of only 40 patients included in the intervention and comparator arm. Accordingly, all effect estimates for patient-relevant endpoints are based on comparatively low case numbers. In particular, the effect estimate on overall survival is based on only 26 events in the intervention arm and 29 events in the comparator arm.

Furthermore, there are imbalances regarding the baseline characteristics of the patients included in the study arms. In particular, 22.5% of the patients in the intervention arm and 42.5% in the comparison arm had an IPI score (International Prognostic Index) of 4–5. A bulky disease was found in 25% of patients in the intervention arm and 37.5% in the comparator arm. Both characteristics are of prognostic relevance, at least in the early lines of therapy. These incidental imbalances could thus lead to a distortion in favour of polatuzumab vedotin in combination with bendamustine and rituximab.

A further relevant uncertainty of the GO29365 study is that the BR scheme used in the comparator arm does not correspond to the currently preferred treatment options for non-transplantable patients in the second-line treatment of r/r DLBCL in the German healthcare context.

Finally, because the GO29365 study cannot provide any statements on morbidity and quality of life regarding, the extent of the additional benefit is limiting.

The extent of the limitations and uncertainties of the study results is considered to be so significant in the overall assessment that, despite the significant advantage in overall survival, it is not possible to quantify the additional benefit overall.

In the overall view, there was a non-quantifiable additional benefit for polatuzumab vedotin in combination with bendamustine and rituximab compared with bendamustine in combination with rituximab in the treatment of adult patients with r/r DLBCL who are ineligible for haematopoietic stem cell transplant because the scientific evidence base does not allow quantification.

Significance of the evidence

The assessment of the additional benefit is based on the randomised, controlled comparison of study arms C (intervention arm) and D (comparison arm) of the pivotal, multi-centre, multi-arm, open Phase Ib/II GO29365 study.

The risk of bias at the study level is estimated to be high. Cross-endpoint limitations with regard to significance result in particular from the small sample size of only 40 patients each included in the intervention and comparator arm.

Furthermore, the study is not blinded.

In addition, detailed information on the statistical evaluations is missing for the endpoints considered in the benefit assessment.

In the overall view, there is a hint for an additional benefit in terms of the significance of the evidence.

2.1.3 Summary of the assessment

The present assessment refers to the benefit assessment of the new medicinal product “Polivy” with the active ingredient polatuzumab vedotin. Polivy was approved as an orphan drug under “special conditions” in the following therapeutic indication: “Polivy in combination with bendamustine and rituximab is indicated for the treatment of adult patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) who are not candidates for haematopoietic stem cell transplant”.

The pharmaceutical company presented data from the pivotal, multi-centre, multi-arm, open-label Phase Ib/II GO29365 study for the benefit assessment. The randomised controlled comparison of polatuzumab vedotin in combination with bendamustine and rituximab compared with bendamustine in combination with rituximab is relevant for the present assessment.

In the endpoint category mortality, there is a statistically significant difference to the advantage of polatuzumab vedotin in combination with bendamustine and rituximab. Compared with treatment with bendamustine in combination with rituximab, there is a significant advantage.

From the results available on the morbidity endpoint complete response and the neuropathy-specific questionnaire TINAS, no conclusions can be drawn about the extent of the additional benefit.

In the study, no data on health-related quality of life were collected. Therefore, no statement can be made about the extent of the additional benefit in terms of quality of life.

The results on side effects do not show any differences relevant to the assessment.

However, relevant limitations and uncertainties of the available study results, in particular because of a small sample size and small number of cases, imbalances between the study arms, and the comparison with a therapy scheme that does not correspond to the currently preferred treatment options do not allow quantification of the additional benefit overall despite the significant advantage in overall survival.

In conclusion, the G-BA found a non-quantifiable additional benefit for polatuzumab vedotin in combination with bendamustine and rituximab compared with bendamustine in combination with rituximab.

In particular because of the small sample size of the GO29365 study, the open study design, and the lack of detailed information on the statistical analyses, there is a hint for an additional benefit results regarding the significance of the evidence.

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 in the dossier and the written statement of the pharmaceutical company. In the present therapeutic indication, this is a heterogeneous patient population consisting of patients with different numbers of previous therapies and different forms of DLBCL. In this respect, only limited epidemiological data are available so that the suitability of some of the sources used is associated with uncertainties or some of the assumptions made by the pharmaceutical company are not comprehensible.

Overall, the number of patients determined in this way is subject to a high degree of uncertainty, which is expressed by the indication of a correspondingly large range.

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 Polivy® (active ingredient: polatuzumab vedotin) at the following publicly accessible link (last access: 9 June 2020):

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

Treatment with polatuzumab vedotin should only be initiated and monitored by specialists in internal medicine, haematology, and oncology experienced in the treatment of patients with diffuse large B-cell lymphoma.

This medicinal product received a conditional marketing authorisation. The EMA will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

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: 1 July 2020).

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”, the time between individual treatments, and the maximum treatment duration if specified in the product information.

For dosages depending on body weight (BW) or body surface, the average body measurements were used as a basis (average body size: 1.72 m, average body weight: 77 kg). From this, a body surface area of 1.90 m² is calculated (calculation according to Du Bois 1916).

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				
Polatuzumab vedotin	On Day 1 of a 21-day cycle	6	1	6
Bendamustine	On Day 1 + 2 of a 21-day cycle	6	2	12
Rituximab	On Day 1 of a 21-day cycle	6	1	6

Usage and consumption:

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					
Polatuzumab vedotin	1.8 mg/kg BW = 138.6 mg	138.6 mg	1 × 140 mg	6	6 × 140 mg
Bendamustine	90 mg/m² = 171.0 mg	171.0 mg	1 × 100 mg + 3 × 25 mg	12	12 × 100 mg + 36 × 25 mg
Rituximab	375 mg/m² = 712.5 mg	712.5 mg	1 × 1400 mg	6	6 × 1400 mg

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Sections 130 and 130 a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. 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.

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					
Polatuzumab vedotin	1 PIC	€ 14,751.37	€ 1.77	€ 860.97	€ 13,888.63
Bendamustine 100 mg	1 PIC	€ 313.05	€ 1.77	€ 24.95	€ 286.33
Bendamustine 25 mg	1 PIC	€ 85.71	€ 1.77	€ 5.70	€ 78.24

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
Rituximab	1 SFI	€ 2,863.08	€ 1.77	€ 164.46	€ 2,696.85
Abbreviations: SFI = solution for injection; PIC = powder for the preparation of an infusion solution concentrate					

Pharmaceutical retail price (LAUER-TAXE®) as last revised: 1 July 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 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.

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	Treatment days/year	Costs/patient/year
Polatuzumab vedotin or rituximab							
Dimetindene i.v. 1 mg/10 kg	5 SFI	€ 18.15	€ 1.77	€ 1.92	€ 14.46	6	€ 43.38
Paracetamol[2] 500–1,000 mg	20 × 500 mg TAB	€ 1.46	€ 0.07	€ 0.06	€ 1.33	6	€ 1.33
Rituximab							
HBV test	-	-	-	-	€ 5.50	1	€ 5.50

2 Non-prescription medicinal products that are reimbursable by the statutory health insurance in accordance with Annex I of the Pharmaceuticals Directive (OTC exemption list) are not subject to the current medicinal product price regulation. Instead, in accordance with Section 129, paragraph 5a SGB V) when a non-prescription medicinal product is sold and invoiced in accordance with Section 300, for the insured person, a pharmaceutical selling price in the amount of the selling price of the pharmaceutical company – plus the surcharges according to Sections 2 and 3 of the Pharmaceutical Price Ordinance in the 31 December 2003 version – shall apply.

Hepatitis B surface antigen status (fee schedule number 32781)							
Hepatitis B antibody status (fee schedule number 32614)	-	-	-	-	€ 5.90	1	€ 5.90
Abbreviations: SFI = solution for injection; TAB = tablets							

Other services covered by SHI funds:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe; contract on price formation for substances and preparations of substances) 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 special agreement on contractual unit costs of retail pharmacist services [Hilfstaxe"] (last revised: 11. Supplementary Agreement of 1 March 2020 to the contract on price formation for substances and preparations of substances), surcharges for the preparation of parenteral preparations containing cytostatics of a maximum of € 81 per ready-to-use preparation and for the preparation of parenteral solutions containing monoclonal antibodies of a maximum of € 71 per ready-to-use unit shall apply. These additional costs are not added to the pharmacy sales price but rather follow the rules for calculating the Hilfstaxe. The cost representation is based on the pharmacy retail 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 ingredients, the invoicing of discards, and the calculation of application containers and carrier solutions according to the regulations of Annex 3 of the Hilfstaxe.

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

On 22 January 2020, the pharmaceutical company submitted a dossier for the benefit assessment of polatuzumab vedotin to the G-BA in due time in accordance with Chapter 5, Section 8, number 1, sentence 2 VerfO.

The benefit assessment of the G-BA was published on 15 May 2020 together with the IQWiG assessment of treatment costs and patient numbers on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. The deadline for submitting written statements was 5 June 2020.

The oral hearing was held on 22 June 2020.

A new version of the G-BA dossier assessment was prepared on 7 July 2020. Version 1.1 of 7 July 2020 replaces version 1.0 of the dossier assessment of 15 May 2020 and was brought

to the attention of the Subcommittee on Medicinal Products at its session on 7 July 2020. The evaluation result was not affected by the changes in version 1.1 compared with version 1.0.

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 28 July 2020, and the proposed resolution was approved.

At its session on 20 August 2020, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	12 May 2020	Information of the benefit assessment of the G-BA
Working group Section 35a	17 June 2020	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	22 June 2020	Conduct of the oral hearing
Working group Section 35a	30 June 2020 14 July 2020	Consultation on the dossier assessment by the G-BA, the assessment of treatment costs and patient numbers by the IQWiG, and the evaluation of the written statement procedure
Subcommittee on Medicinal Products	28 July 2020	Concluding discussion of the draft resolution
Plenum	20 August 2020	Adoption of the resolution on the amendment of Annex XII of the AM-RL

Berlin, 20 August 2020

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

Prof. Hecken