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 Glasdegib (Acute Myeloid Leukaemia (AML), Combination with Cytarabine (LDAC))

of 18 February 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.

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 of the Council of 16 December 1999, the additional medical benefit is considered to be proven through the grant of the marketing authorisation in accordance with 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 12 calendar months. In accordance with 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 in accordance with Chapter 5, Section 5, paragraphs 1–6 VerfO, in particular regarding the additional medical 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 compared 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 glasdegib in accordance with Chapter 5, Section 8, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO) is 15 August 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 7 August 2020.

Glasdegib for the treatment of newly diagnosed de novo or secondary acute myeloid leukaemia (AML) in adult patients 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 assess 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 1 December 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 G20-17) prepared by the IQWiG, and the written statements submitted in the written and oral hearing procedure as well as the amendment to the benefit assessment prepared by the G-BA.

In order to determine the extent of the additional benefit, the G-BA has assessed the studies relevant for marketing authorisation with regard to their therapeutic relevance (qualitative) according to the criteria laid down in Chapter 5, Section 5, paragraph 7, sentence 1, numbers 1–4 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of glasdegib.

In light of the above and taking into account the written 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 glasdegib (Daurismo) in accordance with the product information

Daurismo is indicated, in combination with low-dose cytarabine, for the treatment of newly diagnosed de novo or secondary acute myeloid leukaemia (AML) in adult patients who are not candidates for standard induction chemotherapy.

1 General Methods, Version 6.0 dated 5 November 2020. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care), Cologne.

Therapeutic indication of the resolution (resolution of 18 February 2021):

See approved therapeutic indication

2.1.2 Extent of the additional benefit and significance of the evidence

Adult patients with newly diagnosed de novo or secondary acute myeloid leukaemia (AML) who are not candidates for standard induction chemotherapy

In summary, the additional benefit of glasdegib in combination with low-dose cytarabine (LDAC) is assessed as follows:

Hint for a considerable additional benefit

Justification:

For the benefit assessment of the active ingredient glasdegib, the pharmaceutical company submitted the pivotal, open-label Phase Ib/II study B1371003. This is a completed, multi-centre study conducted in 6 countries and 38 study sites from January 2014 to March 2019. Only the randomised Phase II part of the study is used for the benefit assessment.

Study B1371003 included adult patients (≥ 55 years) with untreated AML or with high-risk myelodysplastic syndrome (MDS). Because of the authorisation status, only the authorisation-compliant sub-population of patients with diagnosed AML who are not suitable for standard induction chemotherapy ("Unfit" population) is relevant for the present benefit assessment. These are patients who have met at least one of the following criteria: Age ≥ 75 years or ECOG-PS of 2 or serum creatinine value of > 1.3 mg/dl or serious cardiological disease.

A total of 132 patients were included in the study; they were randomised in a 2:1 ratio to the glasdegib + LDAC arm (N = 88) or to the LDAC arm (N = 44). In terms of the authorisation-compliant sub-population, there were 78 AML patients in the intervention arm and 38 AML patients in the control arm. Randomisation was stratified by cytogenetic risk profile in accordance with IVRS exclusively in the overall population (AML+MDS) but not for the authorisation-compliant sub-population. As a consequence, comparatively more patients in the glasdegib + LDAC arm had a favourable/intermediate risk (62.8% vs 55.3%). However, with regard to the "Unfit" criteria, there were overall higher proportions of less favourable categories for the glasdegib + LDAC arm.

At the time of study inclusion, patients had a median age of 76 years (glasdegib + LDAC) and 75 years (LDAC). Patients in both study arms received 20 mg LDAC injected subcutaneously twice daily on Days 1–10 of each 28-day cycle. Patients in the intervention arm also received 100 mg of oral glasdegib daily. For the intervention arm, the study duration was generally 12 cycles (1 year) or until a discontinuation criterion occurred. In the control arm, treatment was always continued until a discontinuation criterion occurred. The median duration of exposure for glasdegib + LDAC was 83 days and for LDAC monotherapy, 41 days. The median observation period (for the primary endpoint of the study) was 226 days in the intervention arm and 115 days in the comparator arm.

The primary endpoint of Study B1371003 was overall survival. Furthermore, endpoints on morbidity (including haematological response, cytogenetic response, and transfusion independence) and side effects were surveyed. Endpoints for the health-related quality of life category were not surveyed in the study. For the benefit assessment, the primary data cut-off of 3 January 2017, on which the marketing authorisation is also based, is available.

On the selected comparator

In Study B1371003, monotherapy with LDAC was given in the control arm. According to the written statements of the clinical experts, therapy in the present therapeutic indication is undergoing a change. The standard of therapy in the therapeutic indication includes mainly hypomethylating substances (HMA: azacitidine or decitabine) as well as LDAC, which is used especially in contraindications to HMA. Because of new treatment options that have already been approved or are in the process of being approved, the importance of LDAC monotherapy is currently receding in the view of clinical experts.

In study B1371003, the median treatment time of LDAC monotherapy is shorter compared to other studies. In this regard, in the written statement procedure, the pharmaceutical company and the clinical experts refer to the unfit population of the study in which approx. 55% of the patients in the control arm exhibited > 1 of the aforementioned "unfit" criteria and thus have a comparatively worse prognosis. In accordance with the statements of the clinical experts during the written statement procedure, the "unfit" population corresponds to patients in the reality of care who are not suitable for standard induction therapy.

Mortality

In Study B1371003, overall survival was surveyed as the primary endpoint. Overall survival was defined as the time from randomisation to death regardless of the underlying cause of death. The results for overall survival at the primary data cut-off are considered meaningful.

Treatment with glasdegib + LDAC leads to a statistically significant advantage in overall survival compared with LDAC. The extent of this benefit is also assessed as a significant improvement in overall survival against the background of the known poor prognosis for patients in the therapeutic indication.

Morbidity

Transfusion independence

In Study B1371003, the endpoint transfusion independence is defined as the proportion of patients with transfusion independence of ≥ 8, ≥ 12, ≥ 16, ≥ 20, and ≥ 24 weeks during the treatment phase (i.e. patients were not allowed to receive any transfusion (platelets, red cells, granulocytes or whole blood transfusions) during the defined contiguous periods). Transfusion independence was surveyed post-hoc.

Patients in the present therapeutic indication require frequent and lifelong transfusions.

In the present therapeutic indication, a long-term or sustained avoidance of transfusions (freedom independence) while maintaining a defined minimum haemoglobin value represents a relevant therapy goal with which anaemia and anaemia-related symptoms are controlled with simultaneous freedom EC transfusions.

In Study B1371003, the transfusions are administered according to the practice guidelines of the study centres. Recommendations are also mentioned in the study protocol. However, a uniform guideline with criteria for the administration of transfusions as well as for the collection and documentation of data is lacking; this results in uncertainties regarding the validity of the endpoint. Further uncertainties arise because of limitations in operationalisation.

With regard to the evaluations on the different periods of freedom from transfusion, the G-BA considers a freedom from transfusion of ≥ 24 weeks to be the relevant period in order to be able to assume a long-term avoidance of transfusions (transfusion independence). Thus, transfusion independence ≥ 24 weeks may represent a patient-relevant endpoint in the present therapeutic indication.

However, in the present study B1371003, transfusions were recorded only during the treatment period. This was a median of between 6 (LDAC) and 12 weeks (glasdegib + LDAC) so that after 24 weeks, only a few patients, especially in the LDAC arm, were still receiving therapy. In addition, the remaining survival time (median survival 8.3 months with glasdegib + LDAC vs 4.3 months with LDAC) was also shorter than 24 weeks for many patients in Study B1371003, especially in the comparator arm. Because of this low number of cases and events, an increased uncertainty of results can be assumed.

The results for the endpoint transfusion independence are only presented additionally, taking into consideration the aforementioned uncertainties in operationalisation and validity and, in particular, the low numbers of cases and events. No statement can be derived on the extent of the additional benefit.

Complete response (CR)

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 B1371003 study, the CR endpoint was assessed using the Cheson criteria of 2003 by blood and bone marrow examinations. Thus, the endpoint was not assessed on the basis of symptoms but on the basis of laboratory tests. The data submitted by the pharmaceutical company are also classified as having limited validity because, among other things, no further information is available on the subcomponents transfusion independence and extramedullary manifestation. In addition, transfusion independence is already assessed as a separate endpoint.

The results for the endpoint CR are classified as an endpoint of unclear relevance for the present assessment and are only presented additionally. No statement can be derived on the extent of the additional benefit.

In the overall consideration of the results on morbidity, no statements on the extent of the additional benefit can be derived.

Quality of life

Health-related quality of life was not surveyed in the B1371003 study. No statement on the quality of life can be derived.

Side effects

Total adverse events (AE)

Almost all patients experienced AE. The results for the AE endpoint are only presented additionally.

Severe adverse events (CTCAE grade ≥ 3) and serious adverse events (SAE)

For the endpoints SAE and severe AE (CTCAE grade ≥ 3), there are no statistically significant differences between the treatment arms.

Discontinuation because of AE

With regard to the endpoint discontinuation because of AEs, the pharmaceutical company presented additional evaluations on the endpoint discontinuation because of AEs of at least one active ingredient component within the scope of the written statement procedure. For the

present benefit assessment, the operationalisation as discontinuation of at least one active ingredient component is used for this endpoint.

With regard to the endpoint discontinuation because of AE, there is a significant difference in favour of glasdegib + LDAC. Because of the short observation time in the control arm, which results in particular as a consequence of many deaths, and the many early censorings in the intervention arm, this advantage is subject to uncertainties.

AE of special interest

For the endpoints AE of special interest, there are no statistically significant differences between the treatment arms.

In the overall view of the results of the side effects endpoint category, an advantage can be derived for glasdegib + LDAC compared with LDAC in the endpoint discontinuation because of AE.

Overall assessment

For the benefit assessment of glasdegib in combination with low-dose cytarabine (LDAC) for the treatment of newly diagnosed de novo or secondary acute myeloid leukaemia (AML) in adult patients who are not eligible for standard induction chemotherapy, results for the endpoint categories mortality, morbidity, and side effects are available from the B1371003 study.

Treatment with glasdegib in combination with LDAC resulted in a statistically significant advantage in overall survival compared with LDAC monotherapy; this is considered to be a significant prolongation of life. Against the background of the known poor prognosis for patients in the therapeutic indication, which is also evident in the present B1371003 study through short survival times, the magnitude of the effect of glasdegib + LDAC on survival time is judged to be considerable.

In the overall consideration of the results on morbidity, no statements on the extent of the additional benefit can be derived.

Health-related quality of life was not surveyed in the present study. Statements on quality of life are particularly important in the present palliative therapy situation.

For the side effects endpoint category, an advantage can be derived for glasdegib + LDAC compared with LDAC in the endpoint discontinuation because of AE.

As a result, the G-BA states that in the treatment of adult patients with newly diagnosed de novo or secondary acute myeloid leukaemia (AML) who are not candidates for standard induction chemotherapy, there is considerable additional benefit for glasdegib in combination with LDAC compared with LDAC monotherapy.

Significance of the evidence

This assessment is based on the results of the open-label, partially randomised B1371003 Phase Ib/II study comparing glasdegib + LDAC with LDAC. Only the sub-population of AML patients in the randomised-controlled Phase II part of the study that is compliant with the marketing authorisation is relevant for the benefit assessment.

Basically, the risk of bias is classified as high because of the open study design.

Uncertainties also arise from the LDAC comparator used. According to the statements of the clinical experts, LDAC is one of the standard therapies in the therapeutic indication; however, in the German healthcare context, it is usually less preferable than hypomethylating substances. Furthermore, the treatment duration with LDAC in the comparator arm of study B1371003 is shorter than in comparable studies, thereby resulting in further uncertainty.

In addition, further uncertainties arise from the composition of the patient population. There is a moderate random imbalance in the risk profile to the detriment of the comparator LDAC. In addition, patients < 55 years of age were not included in the study.

With regard to the palliative therapy situation with limited life expectancy in this case, data on health-related quality of life are given high priority. The absence of this data therefore weighs heavily.

For the reasons mentioned above, the reliability of data of the additional benefit identified is classified in the “hint” category.

2.1.3 Summary of the assessment

The present assessment refers to the benefit assessment of the new medicinal product Daurismo with the active ingredient glasdegib. Glasdegib was approved as an orphan drug. Glasdegib in combination with low-dose cytarabine (LDAC) is approved for the treatment of newly diagnosed de novo or secondary acute myeloid leukaemia (AML) in adult patients who are not candidates for standard induction chemotherapy.

For the benefit assessment, results are available from the open-label, partly randomised-controlled Phase Ib/II Study B1371003, which compared glasdegib + LDAC with LDAC. Relevant for the benefit assessment is the sub-population of the Phase II part of the study that is compliant with the marketing authorisation.

Results for the endpoint categories mortality, morbidity, and side effects are available.

In terms of overall survival, there is a clear advantage for glasdegib + LDAC; this is considered considerable against the background of the known poor prognosis for patients in the therapeutic indication.

In the overall consideration of the results on morbidity, no statements on the extent of the additional benefit can be derived.

Health-related quality of life was not surveyed in the present study.

For the side effects endpoint category, an advantage can be derived for glasdegib + LDAC compared with LDAC in the endpoint discontinuation because of AE.

Uncertainties arise because of the open study design as a result of imbalances in the risk profile between the treatment arms, the comparatively short treatment duration of LDAC in the comparator arm, and missing data on health-related quality of life.

In the overall assessment of the results available on the patient-relevant endpoints, the G-BA found a hint for a considerable additional benefit for glasdegib in combination with LDAC for the treatment of adult patients with newly diagnosed de novo or secondary acute myeloid leukaemia (AML) who are not candidates for standard induction chemotherapy.

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

<u>Adult patients with newly diagnosed de novo or secondary acute myeloid leukaemia (AML) who are not candidates for standard induction chemotherapy</u>

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

The G-BA bases its resolution on the patient numbers stated by the pharmaceutical company in the dossier.

The information in the dossier tends to be underestimated. This is largely because the proportion of patients who are not eligible for standard induction therapy tends 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 Daurismo (active ingredient: glasdegib) at the following publicly accessible link (last access: 20 November 2020):

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

Treatment with glasdegib should only be initiated and monitored by specialists in internal medicine, haematology, and oncology who are experienced in the treatment of patients with acute myeloid leukaemia.

Glasdegib can cause embryo-foetal death or severe birth defects when administered to pregnant women. Pregnant women should be informed of the possible risk to the foetus. Glasdegib should not be used in pregnant women and women of childbearing potential who are not using contraception. Women of childbearing age should be advised to use effective contraception at all times during treatment with glasdegib and for at least 30 days after the last dose.

Glasdegib can pass into the semen. Male patients with female partners should be advised of the possible risk of exposure via semen. At all times during treatment with glasdegib and for at least 30 days after the last dose, such patients should be advised to use effective contraception, including a condom (with spermicide if available), even after a vasectomy, in order to prevent exposure of a pregnant or childbearing partner. Men should seek advice on effective fertility preservation before starting treatment with glasdegib.

In accordance with to the requirements of the EMA regarding additional risk minimisation measures, the pharmaceutical company must ensure that all male patients are provided with a patient card by their prescribing doctors for the reasons mentioned above.

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 February 2021).

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 different for each individual patient 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.

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				
Glasdegib	1 × daily	365	1	365
Cytarabine	2 × daily on Day 1–10 of a 28-day cycle	13	10	130

Usage and consumption:

Designation of the therapy	Dosage/appl ication	Dose/patient /treatment day	Consumptio n by potency/treat ment day	Treatment days/ patient/ year	Annual average consumption by potency
Medicinal product to be assessed					
Glasdegib	100 mg	100 mg	1 × 100 mg	365	365 × 100 mg
Cytarabine	20 mg	40 mg	1 × 40 mg	130	130 × 40 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 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined based on consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated based on 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 Sectio n 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Glasdegib 100 mg	30 FCT	€ 13,776.64	€ 1.77	€ 783.51	€ 12,991.36
Cytarabine 40 mg	10 SFI	€ 35.07	€ 1.77	€ 1.14	€ 32.16
Abbreviations: FCT = film-coated tablets; SFI = solution for injection					

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.

No additionally required SHI services are taken into account for the cost representation.

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; Sections 4 and 5 Pharmaceutical Price Ordinance) of 1 October 2009 is not fully used to calculate the 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 *Hilfstaxe* in its currently valid version, surcharges for the production of parenteral preparations containing cytostatic agents of a maximum of € 81 per ready-to-use preparation and for the production of parenteral solutions containing monoclonal antibodies of a maximum of € 71 per ready-to-use unit are to be payable. 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 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 sales price of the active ingredient, the invoicing of discards, the calculation of application containers and carrier solutions according to the regulations in 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 7 August 2020, the pharmaceutical company submitted a dossier for the benefit assessment of glasdegib to the G-BA in due time in accordance with Chapter 5, Section 8, number 1, sentence 1 VerfO.

At its session on 6 October 2020, the Subcommittee on Medicinal Products agreed to postpone the publication of the dossier assessment from 16 November 2020 to 1 December 2020. This postponement was not due to a late submission of the dossier for the benefit assessment but rather to a delay in making the dossier assessment available.

The benefit assessment of the G-BA was published on 1 December 2020 together with the IQWiG assessment of treatment costs and patient numbers on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. The deadline for submitting

written statements was 22 December 2020.

The oral hearing was held on 11 January 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 9 February 2021, and the proposed resolution was approved.

At its session on 18 February 2021, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	24 November 2020	Information of the benefit assessment of the G-BA
Working group Section 35a	5 January 2021	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	11 January 2021	Conduct of the oral hearing
Working group Section 35a	19 January 2021 2 February 2021	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	9 February 2021	Concluding discussion of the draft resolution
Plenum	18 February 2021	Adoption of the resolution on the amendment of Annex XII of the AM-RL

Berlin, 18 February 2021

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

Prof. Hecken