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 Gilteritinib (Relapsed or Refractory Acute Myeloid Leukaemia with an FLT3 Mutation)

of 14 May 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 of 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 in such a way 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 gilteritinib in accordance with Chapter 5, Section 8, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO) is 1 December 2019. 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 27 November 2019.

Gilteritinib for the treatment of acute myeloid leukaemia is approved as a medicinal product for the treatment of a rare disease under Regulation (EC) No 141/2000 of the European Parliament and of 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 2 March 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 evaluation carried out by the G-BA, the assessment of treatment costs and patient numbers (IQWiG G19-20) 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 gilteritinib.

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 gilteritinib (XOSPATA) in accordance with the product information

XOSPATA is indicated as monotherapy for the treatment of adult patients who have relapsed or refractory acute myeloid leukaemia (AML) with an FLT3 mutation.

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

In summary, the additional benefit of gilteritinib is assessed as follows.

A hint for a considerable additional benefit has been shown for gilteritinib as monotherapy for the treatment of adult patients who have relapsed or refractory acute myeloid leukaemia (AML) with a FLT3 mutation.

Justification:

To demonstrate the extent of the additional benefit the pharmaceutical company presents the findings of the pivotal multi-site, open, randomised, controlled phase III study ADMIRAL (2215-CL-0301). The study included patients with acute myeloid leukaemia (AML) with a FLT3 mutation who had relapsed or were refractory to first-line therapy. The patients were between 18 and 85 years old.

A total of 371 patients were enrolled in the ADMIRAL study in a parallel assignment (2:1) with 247 patients randomized to the gilteritinib arm and 124 patients randomized to the salvage chemotherapy arm. In the intervention arm, 246 patients received gilteritinib (120 mg) while 109 patients in the control arm received salvage chemotherapy. Thus, 12% of the patients randomized into the control group (n = 15) did not receive any study medication, while in the gilteritinib arm one person was not treated with the assigned drug. The following options were available for salvage chemotherapy: a) low intensity chemotherapy (low-dose cytarabine (LoDAC) or azacitidine) or b) high intensity chemotherapy (MEC induction chemotherapy (mitoxantrone, etoposide and medium-dose cytarabine) or FLAG-IDA induction chemotherapy (fludarabine, cytarabine and granulocyte colony stimulating factor with idarubicin)). Randomization was stratified based on the pre-selected salvage chemotherapy and the response to first-line therapy. In the opinion of medical experts, the salvage chemotherapy regimens employed in the ADMIRAL study are appropriate in the context of the German healthcare system and, according to the current state of medical knowledge, are predominantly administered with the intent of providing palliative care. Treatment in both the gilteritinib arm and with low-dose salvage chemotherapy was administered in continuous 28-day cycles until a predetermined criterion for discontinuation of treatment was reached. High-dose salvage chemotherapy was administered in a 28-day cycle. On or after day 15, response to this treatment was evaluated on the basis of institutional guidelines. Depending on the response, treatment was extended with a second cycle.

The most frequent reasons for discontinuing the designated treatment were disease progression, followed by lack of efficacy and death. Once the study treatment was completed, long-term follow-up was performed every 3 months for up to 3 years after the end of treatment.

Patients in the gilteritinib arm were able to receive haematopoietic stem cell transplantation (HSCT) during the study period, for that time gilteritinib treatment was suspended. Afterwards, the patients could be further treated with gilteritinib. In patients receiving salvage chemotherapy, HSCT was performed only after discontinuation of chemotherapy and was, therefore, recorded exclusively as follow-up therapy. These treatment schemes meant that treatment duration with the study medication varied between the treatment arms.

The median age of patients in the ADMIRAL study was 61.5 (gilteritinib) and 62 years (salvage chemotherapy). The ECOG performance status of most patients was grade 0 to 1 (83.4% and 84.7%) and most had an internal tandem duplication (FLT3-ITD) (87.0% and 91.1%). In contrast, 8.5% and 8.1% of patients in each arm had an FLT3 mutation in the tyrosine kinase domain (FLT3-TKD), and 2.5% and 0% had both mutation types. In 1.6% and 0.8% of patients in each arm, it was not possible to determine a mutation status based on a central assessment.

Midostaurin is a tyrosine kinase inhibitor that is already available for patients with a FLT3 mutation. In the G-BA's benefit assessment, this drug was found to be associated with a considerable additional benefit in first-line treatment of AML and can be employed in

healthcare. In the ADMIRAL study, 13 patients in the intervention arm (5.3%) and 8 patients in the control arm (6.5%) were pretreated with midostaurin.

The on-going ADMIRAL trial is being conducted in 107 study sites in 14 countries in Europe, North America, Asia and the rest of the world. Patients were recruited between October 2015 and February 2018. The final confirmatory analysis was scheduled to be undertaken when 258 events occurred in the overall survival endpoint. The results of this final analysis dated 17 September 2019 are used for the present assessment.

The ADMIRAL study only partially covers the use of gilteritinib in the therapeutic indication, as patients with more than one previous therapy were not included in the study. Hence, gilteritinib's marketing authorisation in the present indication was based not only on the ADMIRAL study but also on the single-arm, multi-site phase I/II study CHRYSALIS (2215_CL-0101), in which patients with up to three previous AML therapies were included.

Mortality

In the ADMIRAL study, overall survival was defined as the time from randomisation to death from any cause. Survival status was assessed by telephone during the follow-up period, initially 30 days after the end-of-treatment consultation and subsequently every 3 months for up to 3 years after the end of treatment. Treatment with gilteritinib resulted in a statistically significant advantage in overall survival compared with salvage chemotherapy (hazard ratio (HR) = 0.64; 95% CI (0.49; 0.83), p value = 0.0007). The median survival time for gilteritinib is 9.3 (7.7; 10.7) months compared to 5.6 (4.7; 7.3) months for salvage chemotherapy, an increase of 3.7 months in median overall survival.

Sensitivity analyses confirm the finding. The statistically significant advantage of gilteritinib over salvage chemotherapy is particularly marked in the stratified analysis with censored data for patients treated with HSCT and the unstratified analysis with censored data for patients receiving follow-up therapy.

Treatment with gilteritinib results in a moderate improvement in overall survival compared to the previously employed therapy regimens. Patients in the therapeutic indication are known to have a poor prognosis, as evidenced by the short survival times in the ADMIRAL study. Against this background, gilteritinib is considered to be associated with a significant improvement in survival time.

Morbidity

Remission

The complete remission (CR) endpoint is an important prognostic factor and relevant for therapeutic decision. A CR associated with a noticeable decrease in disease symptoms for the patient is always relevant for the benefit assessment. In the ADMIRAL study, the CR endpoint was assessed using the Cheson criteria by examination of blood and bone marrow. Thus, the endpoint was not assessed on the basis of symptoms but on the basis of laboratory tests. In addition, the data submitted by the pharmaceutical company are deemed to be invalid, as a significant bias must be assumed due to missing data, especially in the control arm. The findings for the remission endpoint are not used in this assessment.

Rate of haematopoietic stem cell transplantations

Regarding the rate of haematopoietic stem cell transplantations (HSCT), a statistically significant advantage to the benefit of gilteritinib has been demonstrated. 25.5% of patients in the gilteritinib arm and 15.3% of patients in the salvage chemotherapy arm received HSCT. These figures represent both HSCT received during the study period (in the gilteritinib arm) and HSCT received as a follow-up therapy (primarily after salvage chemotherapy).

This endpoint cannot be drawn on to make conclusions on the patient-relevant therapeutic effects of gilteritinib, due to a lack of information on the conditions or reasons for or against the administration of HSCT, and due to the differences in operationalisations in the treatment

arms. The endpoint is a relevant clinical parameter and, therefore, presented as supplementary information in the benefit assessment. It cannot be used to assess the extent of the additional benefit.

Patient reported endpoints

For record patient-reported morbidity endpoints, the Brief Fatigue Inventory (BFI) questionnaire, items related to leukaemia-specific symptoms, the Functional Assessment of Chronic Illness Therapy – Dyspnea-Short Form (FACIT-Dys-SF) questionnaire, and the visual analogue scale of the EuroQol 5-dimensional questionnaire (EQ-5D-VAS) were used in the ADMIRAL study.

In the gilteritinib arm, > 70% of patients completed the questionnaires (with the exception of FACIT-Dys-SF) at the beginning of the second and third therapy cycle. In the control group, in contrast, the response rates at the beginning of the second therapy cycle were only 10–13%. Due to the very high percentage of missing data and the large difference between the two study arms, the findings for these endpoints are not valid and cannot be used for the benefit assessment. The data on patient-reported endpoints to assess morbidity cannot be used to draw conclusions on the extent of the additional benefit.

Quality of life

Quality of life was assessed in the ADMIRAL study using the Functional Assessment of Cancer Therapy – Leukaemia (FACT-Leu) instrument. Similar to the patient-reported morbidity endpoints, the FACT-Leu response rate in the control group was so low and the difference in both treatment arms so large that no valid findings can be derived. Thus, the extent of additional benefit cannot be deduced from the findings for this endpoint.

Side effects

In the side effects endpoint category, there were relevant variations in the observation period due to the different treatment durations in the two therapeutic arms, and, hence, these findings are associated with uncertainties. The principal problem is the short treatment duration in the control arm, resulting in frequent early censoring of data in the control arm. For this reason, only the event-time analyses are used for the benefit assessment, on the basis of which comparative conclusions can only be inferred for the period of the first two months of therapy.

Adverse events (AEs)

Almost all patients experienced adverse events (AEs). The results for the AE endpoint are therefore presented only on a supplementary basis.

Serious adverse events (SAEs)

The event-time analyses reveal a statistically significant effect to the detriment of gilteritinib. It should be noted that the median time to event in the control arm is primarily due to frequent early censoring. For this reason, the data on SAEs are subject to a very high degree of uncertainty.

Severe adverse events (CTCAE grade ≥ 3)

A statistically significant benefit in favour of gilteritinib was found in the event time analyses. The effect is very small, with a median time to the first event of 0.3 months in the gilteritinib arm and 0.2 months in the control arm, and the extent of the difference is not assessed as sufficiently relevant.

Discontinuation due to AEs

Regarding the discontinuation due to AEs endpoint, the event-time analyses reveal a significant effect in favour of gilteritinib. However, due to the short observation time and frequent early censoring, this advantage in favour of gilteritinib is associated with a very high degree of uncertainty.

AEs of special interest

In detail, no statistically significant effects to the detriment of gilteritinib have been presented for the pre-specified AEs of special interest, with the exception of “increase in keratin phosphokinase” and “increase in liver transaminase”. The event-time analyses of the AEs of special interest have been performed for all degrees of severity, and, as a consequence, the relevance of the events is unclear.

In summary, due to the short period of observation in the comparator arm, on the basis of the event time analyses it is only possible to arrive at comparative conclusions for the period of the first two months of therapy. Furthermore, the high censoring count makes interpreting the results problematic. Comparative conclusions regarding longer-term side effects cannot be made on the basis of the data. In aggregate, no valid conclusions can be drawn on the basis of the available data in side effects of gilteritinib compared to salvage chemotherapy.

Thus, overall the side effects endpoint category neither benefits nor detriments have been established for gilteritinib.

Overall assessment

The benefit assessment of gilteritinib as monotherapy for the treatment of adult patients who have relapsed or refractory acute myeloid leukaemia (AML) with a FLT3 mutation draws on findings from the ADMIRAL study in the endpoint categories mortality, morbidity, quality of life and side effects.

Treatment with gilteritinib resulted in a statistically significant benefit in overall survival compared to salvage chemotherapy. This is assessed as a moderate extension of lifespan. Patients in the therapeutic indication are known to have a poor prognosis, as evidenced by the short survival times in the ADMIRAL study. Against this background, gilteritinib is considered to be associated with a significant improvement in survival time.

Due to the large amount of missing data, especially in the salvage chemotherapy arm, and, hence, the large differences between the treatment arms, assessing the effect of gilteritinib on the patient-reported morbidity endpoints is not feasible.

Similar to the case for the patient-reported morbidity endpoints, due to the large amount of missing data, especially in the salvage chemotherapy arm, and, hence, the large differences between the treatment arms, no valid data are available for assessing the effect of gilteritinib on health-related quality of life.

Regarding side effects, due to the short period of observation in the comparator arm, on the basis of the event time analyses it is only possible to draw comparative conclusions for the period of the first two months of therapy. Furthermore, the high censoring count makes interpreting the results problematic. Comparative conclusions regarding longer-term side effects cannot be made on the basis of the data. Thus, overall in the side effects endpoint category no benefits or detriments have been established for gilteritinib.

In conclusion, the G-BA finds that there is a considerable additional benefit for gilteritinib compared to salvage chemotherapy for the treatment of adult patients who have relapsed or refractory AML with a FLT3 mutation.

Significance of the evidence

The assessment of the additional benefit is based on the randomised, controlled, multi-site, open, phase III pivotal ADMIRAL study, which is investigating the efficacy and safety of gilteritinib compared with salvage chemotherapy in a rare disease. For the ADMIRAL study, the risk of bias is classified as high at study level. With the exception of overall survival, all the study’s endpoints are associated with uncertainties, due, in particular, to the short observation period in the comparator arm, on account of which comparative data can only be evaluated for the first two months of therapy. In addition, further uncertainties exist due to the large amount of missing data and censoring, especially in the control arm. Furthermore, uncertainties remain

due to the lack of comparative data on the efficacy of gilteritinib in patients with >1 previous therapy and due to the continuation of therapy after HSCT.

In the overall view, the reliability of data provides a hint for an additional benefit.

2.1.3 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product "XOSPATA" with the active ingredient gilteritinib. XOSPATA has been approved as an orphan drug and is administered as monotherapy for the treatment of adult patients who have relapsed or refractory acute myeloid leukaemia (AML) with a FLT3 mutation.

The pharmaceutical company has presented the open-label, randomised, phase III ADMIRAL study comparing gilteritinib with salvage chemotherapy. The ADMIRAL study is appropriate for the benefit assessment. The analysis of the final data cut-off of the ongoing study can be employed to draw conclusions for the endpoint categories overall survival (mortality), morbidity, quality of life and side effects.

A statistically significant, moderate benefit has been demonstrated for gilteritinib over salvage chemotherapy in the overall survival endpoint. No valid data for patient-reported findings have been presented for morbidity and quality of life. In the side effects endpoint category, on aggregate, no conclusions can be drawn regarding the additional benefit or detriment associated with gilteritinib treatment.

A relevant advantage in the mortality category exists, and, hence, the G-BA finds the drug is associated with a considerable additional benefit. With the exception of overall survival, all the study's endpoints are associated with uncertainties, due, in particular, to the short observation period in the comparator arm, on account of which comparative data can only be evaluated for the first two months of therapy. In addition, further uncertainties arise due to the large amount of missing data and censoring, especially in the control arm. Furthermore, uncertainties remain due to the lack of comparative data on the efficacy of gilteritinib in patients with >1 previous therapy and due to the continuation of therapy after HSCT. As a result, only a hint for an additional benefit can be derived with regard to the reliability of data.

In conclusion, the G-BA finds that there is a hint for a considerable additional benefit for gilteritinib compared to salvage chemotherapy for the treatment of adult patients who have relapsed or refractory AML with an FLT3 mutation.

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

In general, the figures in the dossier are comprehensible. They are subject to uncertainties due, among other things, to critical calculations of percentages. In addition, the number of patients calculated would be higher if more recent figures on the incidence of AML were employed.

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 XOSPATA (active ingredient: gilteritinib) at the following publicly accessible link (last access: 27 February 2020):

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

Treatment with gilteritinib 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.

According to the requirements for risk minimisation activities in the EPAR (European Public Assessment Report), the pharmaceutical company must provide the following information material on gilteritinib:

- Training material for doctors
- Patient card

FLT3 proof

Before taking gilteritinib, patients with relapsed or refractory AML must be confirmed by means of a validated test as having the FMS-like tyrosine kinase 3 (FLT3) mutation (internal tandem duplications (ITD) or mutations in the tyrosine kinase domain (TKD)).

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

The recommended starting dose is 120 mg gilteritinib (three 40 mg tablets) once daily. If no response is observed after four weeks of treatment (patient does not achieve CRc), the dose may be increased to 200 mg (five 40 mg tablets) once daily if tolerated or clinically appropriate.

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				
Gilteritinib	continuously, 1 × daily	365	1	365

Usage and consumption:

Designation of the therapy	Dosage/application	Dose/patient/treatment day	Consumption by potency/treatment day	Treatment days/ patient/ year	Annual average consumption by potency
Medicinal product to be assessed					
Gilteritinib	120 mg	120 mg	3 × 40 mg	365	1095 × 40 mg
	200 mg	200 mg	5 × 40 mg	365	1825 × 40 mg

Costs:

Costs of the medicinal product:

Designation of the therapy	Package size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Gilteritinib	84 FCT	€ 22,732.83	€ 1.77	€ 1,295.00	€ 21,436.06
Abbreviations: FCT = film-coated tablets					

Pharmaceutical retail price (LAUER-TAXE®) as last revised: 15 April 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 medical treatment or the prescription of other services when using 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.

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 27 November 2019, the pharmaceutical company submitted a dossier for the benefit assessment of gilteritinib 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 02 March 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 23 March 2020.

The oral hearing was held on 6 April 2020.

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

The evaluation of the written statements received and the oral hearing were discussed at the session of the subcommittee on 5 May 2020, and the proposed resolution was approved.

At its session on 14 May 2020, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal Products	25 February 2020	Information of the benefit assessment of the G-BA
Working group Section 35a	1 April 2020	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal Products	6 April 2020	Conduct of the oral hearing
Working group Section 35a	16 April 2020; 29 April 2020	Consultation on the dossier evaluation by the G-BA, the assessment of treatment costs and patient numbers by the IQWiG, and the evaluation of the written statement procedure
Subcommittee Medicinal Products	5 May 2020	Concluding discussion of the draft resolution
Plenum	14 May 2020	Adoption of the resolution on the amendment of Annex XII of the AM-RL

Berlin, 14 May 2020

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

Prof. Hecken