Gemeinsamer Bundesausschuss

Justification

of 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 Olaparib (new therapeutic indication: Adenocarcinoma of the pancreas, BRCA1/2-mutations, maintenance treatment)

of 3 June 2021

Contents

1. Legal basis

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

1st approved therapeutic indication,

2nd medical benefits,

3rd Additional benefit of the medicinal product in relation to the appropriate comparator therapy

4th Number of patients and patient groups for whom there is a therapeutically significant additional benefit,

5th Costs of therapy for the statutory health insurance,

6th Requirements for a quality-assured application.

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

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

2. Key points of the resolution

The active ingredient olaparib (Lynparza) was listed for the first time in the Great German Specialties Tax (Lauer Tax) on 1 June 2015.

On 3 July 2020, olaparib received marketing authorisation for a new therapeutic indication to be classified as a major type 2 amendment as defined according to Annex 2 number 2 letter a) to Regulation (EC) No. 1234/2008 of the commission of 24 November 2008 concerning the examination of amendments to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12 December 2008, p. 7).

On 4 June 2020, the pharmaceutical company submitted an application to merge the evaluation procedures of olaparib according to Section 35a, paragraph 5b SGB V. At its session on 2 July 2020, the G-BA approved the request for merger.

On the 30 November 2020, at the latest within four weeks after the disclosure, the pharmaceutical company on the marketing authorisation of a new therapeutic indication, the pharmaceutical company has submitted a dossier in accordance with Section 4, paragraph 3, number 2 Ordinance of the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient olaparib with a new therapeutic indication "Lynparza® is indicated as monotherapy for the maintenance treatment of adult patients with germline BRCA1/2-mutations who have metastatic adenocarcinoma of the pancreas and whose disease has not progressed after a minimum of 16 weeks of platinum treatment as part of first-line chemotherapy regimen".

The G-BA commissioned IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 15 March 2021 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. An oral hearing was also held.

The G-BA came to a resolution on whether an additional benefit of olaparib compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure. In order to determine the extent of the additional benefit, the G-BA has assesses the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5, Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of olaparib.

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

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

2.1.1 Approved therapeutic indication of olaparib (Lynparza) in accordance with the product information

Lynparza is indicated as monotherapy for the maintenance treatment of adult patients with germline BRCA1/2-mutations who have metastatic adenocarcinoma of the pancreas and have not progressed after a minimum of 16 weeks of platinum treatment within a first-line chemotherapy regimen.

Therapeutic indication of the resolution (resolution of 3/07/2021):

"see approved therapeutic indication"

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

1 General Methods, version 6.0 of 5.11.2020. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

Adult patients with germline BRCA1/2-mutations who have metastatic adenocarcinoma of the pancreas and have not progressed after minimum of 16 weeks of platinum treatment within a first-line chemotherapy regimen as maintenance treatment

Appropriate comparator therapy:

Monitoring wait-and-see approach

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

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

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

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

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

on 1.

In terms of authorisation status, the active ingredients available for the treatment of patients with metastatic adenocarcinoma of the pancreas are 5-fluorouracil, erlotinib, gemcitabine, liposomal irinotecan, mitomycin and nab-paclitaxel, but no medicinal products specifically for the maintenance treatment of pancreatic carcinoma. In addition, folinic acid (Leucovorin) is approved in combination with 5-fluorouracil.

The marketing authorisation of erlotinib and nab-paclitaxel each refers to combination therapy with gemcitabine. Liposomal irinotecan is approved as combination therapy with 5-fluorouracil and leucovorin.

on 2.

For the present therapeutic indication, a non-medicinal treatment is not considered as an appropriate comparator therapy.

on 3.

For the present therapeutic indication there are no resolutions or guidelines of the G-BA for medicinal applications or non-medicinal treatments.

on 4.

The general state of medical knowledge, on which the finding of the G-BA is based, was illustrated by a systematic research for guidelines as well as reviews of clinical studies in the present therapeutic indication.

In principle, the treatment of metastatic adenocarcinoma of the pancreas is palliative, so that there are no curative therapeutic approaches. Regarding platinum treatment within a first-line chemotherapy regimen, for example in the form of the FOLFIRINOX regimen (5-fluorouracil, folinic acid, irinotecan, and oxaliplatin), all present guidelines recommend it exclusively for patients with a favourable risk profile (including ECOG PS 0-1, age ≤ 75 years, normal bilirubin level). Data on the duration of platinum treatment within a first-line chemotherapy regimen for patients whose disease has not progressed on therapy are very limited. Depending on the side effects and the response, there are, among other things, the options to continue therapy until tumour progression (modified if necessary), to interrupt (interval therapy) or to discontinue.

From this point of view, in the present therapeutic indication, it is assumed that first-line chemotherapy is completed or that continuation of first-line chemotherapy is not indicated at the time of the therapeutic decision for olaparib.

The evidence for the specific treatment setting of maintenance treatment for patients with metastatic adenocarcinoma of the pancreas whose disease has not progressed on a minimum of 16 weeks ofplatinum treatment within a first-line chemotherapy regimen is extremely limited. Systematic reviews of maintenance treatment after platinum treatment within first-line chemotherapy for metastatic adenocarcinoma of the pancreas are not available. The guidelines contain no or only very limited statements, with neither a specific recommendation for an active ingredient nor a general recommendation for the implementation of maintenance treatment.

Based on the fact that patients in the present therapeutic indication do not receive a specific therapy according to the current state of medical knowledge, a monitoring wait-and-see approach represents the appropriate comparator therapy.

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

2.1.3 Extent and probability of the additional benefit

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

For adult patients with germline BRCA1/2-mutations who have metastatic adenocarcinoma of the pancreas and whose disease has not progressed after a minimum of 16 weeks of platinum treatment within a first-line chemotherapy regimen, for maintenance treatment, the additional benefit is not proven.

Justification:

The benefit assessment is based on the results of the double-blind, randomised, multi-centre POLO study comparing olaparib with placebo. The study enrolled adult patients with metastatic adenocarcinoma of the pancreas and gBRCA1 and/or gBRCA2 mutation who were previously treated with a minimum of 16 weeks of platinum treatment within a first-line chemotherapy (without interruption) and who, in the opinion of the principal investigators,

had not shown progression. The general condition of the patients should correspond to an Eastern Cooperative Oncology Group Performance Status (ECOG-PS) of 0 or 1.

The POLO study enrolled 154 patients and assigned them in a 3:2 ratio to treatment with either olaparib (92 patients) or placebo (62 patients).

Study treatment was administered as specified in the requirements in the product information and continued until radiographic progression according to RECIST criteria version 1.1, unacceptable toxicity, or death.

The primary endpoint of the POLO study is progression-free survival (PFS). Patient-relevant secondary endpoints are Overall survival, Symptomatology, Health status, Health-related quality of life and Adverse events (AEs).

The primary data cut-off of the Polo study (DCO1) dated 15/1/2019 was used for the benefit assessment. The pre-specified final overall survival data cut-off dated 21/7/2020 (DCO2) was submitted with the statement by the pharmaceutical company. It remains unclear why the final data cut-off (DCO2) was not already prepared in the dossier for the benefit assessment.

On the significance of the study:

At the study level, the overall risk of bias of the study is considered to be low. At the endpoint level, the risk of bias is considered high for all endpoints except Overall survival and Discontinuation due to AE. The reasons for this are the strongly decreasing returns of the questionnaires on the patient-reported endpoints as well as the different observation phases between the treatment groups. For the endpoint Discontinuation due to AEs, the certainty of results is limited despite a low risk of bias, because after premature discontinuation of treatment for other reasons (e.g. progress), Discontinuation due to AEs can no longer occur (competing event).

Uncertainties also exist due to missing data on the reasons for termination of first-line chemotherapy regimen of patients included in the POLO study. This leaves it unclear whether the respective first-line chemotherapy was completed or prematurely discontinued. According to the current state of medical knowledge and recommendations, patients should be treated for 6 months or until progression. However, in the POLO study, 65% of patients were treated ≤ 6 months with first-line chemotherapy. Overall, it is therefore questionable whether the continuation of first-line chemotherapy was actually no longer indicated at the time of randomisation, as required.

Extent and probability of the additional benefit

Mortality

Taking into account the particularly poor prognosis of patients with adenocarcinoma of the pancreas, the overall survival in the therapeutic indication is of particular relevance from the perspective of the G-BA. However, Overall survival is unfortunately only a secondary endpoint in the Polo study.

There was no statistically significant difference between the two treatment arms with respect to the Overall survival endpoint. With olaparib, this event occurred in 41 patients (44.6%) and

with placebo in 30 patients (48.4%). For the endpoint Overall survival, an additional benefit of olaparib is therefore not proven.

Morbidity

Progression-free survival

Progression-free survival (PFS) was the primary endpoint in the POLO study and defined as the time from randomisation to the onset of radiographic progression according to RECIST criteria version 1.1 or death. PFS was statistically significantly prolonged in the olaparib arm compared to the control group.

The PFS endpoint is a combined endpoint composed of endpoints of the mortality and morbidity categories. The endpoint component "Mortality" was collected in the POLO study via the endpoint "Overall survival" as an independent endpoint. The morbidity component "Disease progression" was assessed solely by means of imaging procedures (radiologically determined disease progression according to the RECIST V1.1 criteria). Therefore, morbidity is not primarily assessed on the basis of disease symptoms, but solely on the basis of asymptomatic findings that are not directly relevant to the patient. Taking into account the aspects mentioned above, there are different opinions within the G-BA regarding the patient relevance of the endpoint PFS.

Because radiologically determined disease progression may be associated with effects on morbidity and/or quality of life, available data on morbidity and health-related quality of life will be used to further interpret PFS results. Data on morbidity and health-related quality of life are potentially relevant in this regard, especially when, as in the present case, radiologically determined disease progression is associated with effects on morbidity and/or quality of life.

The prolonged PFS with olaparib was not associated with a benefit in terms of morbidity or quality of life in the POLO study, but there were disadvantages for olaparib in terms of symptomatology in the endpoint Nausea and Vomiting. It should be noted that the corresponding endpoints were only collected up to 30 days after progression. However, robust analysis of data before and after the time of radiologically determined progression are required to assess any impact of radiologically determined progression on quality of life as well as morbidity. In summary, the available data do not indicate that the statistically significant increase in progression-free survival time with olaparib is associated with an improvement in morbidity or health-related quality of life. The results for the endpoint PFS are therefore not used in the present assessment.

Symptomatology

In the POLO study, patients' symptoms were assessed using the symptom scales of the EORTC QLQ-C30 questionnaire and the EORTC QLQ-PAN26 questionnaire specific to adenocarcinoma of the pancreas. The observation period for this was only the period of treatment with the study medication (plus 30 days). In each case, the time to confirmed clinically relevant deterioration of ≥ 10 points at 2 consecutive visits was used for the benefit assessment.

For the endpoint Nausea and vomiting, there is a statistically significant difference to the disadvantage of olaparib compared to sorafenib.

Health status according EQ-5D VAS

Health status was assessed in the POLO study using the EQ-5D visual analogue scale (VAS). The assessment was conducted up to 30 days after the last study medication.
No statistically significant mean difference was detected between the treatment arms.

Quality of life

Health-related quality of life was assessed using the functional scales of the EORTC QLQ-C30 and EORTC QLQ-PAN26 questionnaires, operationalised as time to confirmed clinical worsening by ≥ 10 points at 2 consecutive visits. The assessment was conducted up to 30 days after the last study medication.

Overall, there were no significant advantages or disadvantages for olaparib in the endpoint category Health-related quality of life compared to monitoring wait-and-see approach in the overall study population.

There is an effect modification in the endpoint Physical function based on the feature Age. For the endpoint Infections and infestations, there is a statistically significant difference to the disadvantage of olaparib compared to placebo in patients ≥ 65 years. For the endpoint Hospitalisation no statistically significant difference was detected between the treatment groups in patients < 65 years. However, as the observed effect modification cannot be conclusively assessed, it is not taken into account in the assessment of the additional benefit.

Side effects

Adverse events (AEs in total)

In the POLO study, 95.6% of patients in the intervention arm and 93.3% of patients in the comparator arm experienced an adverse event. The results for the endpoint Total adverse events are only presented supplementary.

Serious AEs

With regard to patients affected by serious AEs, the time-to-event analysis showed no statistically significant difference between the treatment arms.

Severe adverse events (CTCAE grade 3 or 4)

There is no statistically significant difference between the treatment arms in the Polo study.

Discontinuation due to AE

In the time-to-event analysis, there was no statistically significant difference between the treatment groups for the endpoint Discontinuation due to AE.

Specific AE

For the specific AE myelodysplastic syndrome (PT, AE), acute myeloid leukaemia (PT, AE), and pneumonitis (PT, AE) no usable data are available.
For the endpoint Decreased appetite (PT, AE), the time-to-event analysis show a statistically significant difference to the disadvantage of olaparib compared to placebo. There is a possible qualitative overlap with the endpoint Nausea and vomiting of the endpoint category Symptomatology.

Overall assessment

For the benefit assessment of olaparib as monotherapy for the maintenance treatment of adult patients with germline BRCA1/2-mutations who have metastatic adenocarcinoma of the pancreas and whose disease has not progressed after at least 16 weeks of platinum treatment within a first-line chemotherapy regimen, results from the POLO study are available on overall survival, morbidity, health-related quality of life, and side effects compared with monitoring wait-and-see approach, operationalised as placebo. The primary data cut-off (DCO1) is used for the benefit assessment.

Due to the particularly poor prognosis, special importance is attached to overall survival in the therapeutic indication. There is no statistically significant difference in survival time analysis between olaparib and monitoring wait-and-see approach. An additional benefit of olaparib for overall survival is therefore not proven.

In the Morbidity endpoint category, the Nausea and vomiting symptom endpoint showed a statistically significant difference to the disadvantage of olaparib compared to placebo. This disadvantage is assessed as relevant, which is why a disadvantage is identified with regard to morbidity overall.

In the endpoint category Quality of life, there were no significant advantages or disadvantages for olaparib compared to monitoring wait-and-see approach.

In the endpoint category Side effects, there were no significant differences between the treatment arms of the Polo study for the SAEs, Severe AEs (CTCAE grade ≥ 3) and discontinuation due to AEs. In particular, for the endpoint Decreased appetite (PT, AE), there is a statistically significant difference to the disadvantage of olaparib compared to placebo. Overall, neither an advantage nor a disadvantage can be determined for the side effects.

In the overall assessment, the disadvantage in the endpoint category Morbidity is not judged to be so serious that it would justify the finding of a lower benefit overall. Therefore, it is concluded that there is no evidence of an additional benefit of olaparib compared with monitoring wait-and-see approach.

Taking into account the severity of the disease and the opinions of the medical societies on the current reality of care, olaparib may represent a relevant therapeutic option for patients with adenocarcinoma of the pancreas.

2.1.4 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient Olaparib.

The therapeutic indication assessed here is as follows:
Lynparza is indicated as monotherapy for the maintenance treatment of adult patients with germline BRCA1/2-mutations who have metastatic adenocarcinoma of the pancreas and have not progressed after a minimum of 16 weeks of platinum treatment within a first-line chemotherapy regimen.

The G-BA determined the monitoring wait-and-see approach as the appropriate comparator therapy.

For the benefit assessment, the pharmaceutical company presents the randomised, controlled trial POLO, in which olaparib was compared with placebo. Results for the primary data cut-off (DCO1) on overall survival, morbidity, health-related quality of life and side effects were used for the evaluation.

Compared to monitoring wait-and-see approach, operationalised as placebo, there was no statistically significant difference in overall survival for treatment with olaparib. An additional benefit of olaparib for overall survival is therefore not proven.

In the Morbidity endpoint category, the Nausea and vomiting symptom endpoint showed a statistically significant difference to the disadvantage of olaparib compared to placebo. This disadvantage is assessed as relevant, but this does not lead to a downgrading in the overall statement on the additional benefit.

In the endpoint category Quality of life, there were no significant advantages or disadvantages for olaparib compared to monitoring wait-and-see approach.

In the endpoint category Side effects, there were no significant differences between the treatment arms for the endpoints SAEs, severe AEs (CTCAE grade ≥ 3) and discontinuation due to AEs. Specifically, for the endpoint Decreased appetite (PT, AE), there is a statistically significant difference to the detriment of olaparib.–Overall, neither an advantage nor a disadvantage can be determined for the side effects.

Therefore, the additional benefit is not proven.

Olaparib may represent a relevant therapeutic option in the present therapeutic indication.

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

approx. 25 to 75 patients

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

The patient numbers stated in the pharmaceutical company's dossier are an overall underestimation. To counteract this underestimation, two calculation steps were changed, and the patient numbers were recalculated for the present resolution.

In doing so, step 2 of the calculation performed by the pharmaceutical company was adapted to determine the patients with adenocarcinoma of the pancreas. The pharmaceutical

company estimated a proportion value of 95% for adenocarcinoma. The publication of Hermann & Kraywinkel[2] referred to by the pharmaceutical company shows lower percentages for ductal adenocarcinomas and unspecific/other adenocarcinomas, which in total amount to 72.2% (women) and 75.2% (men). If these are weighted with the gender-specific incidence rates (females: 23.48; men: 25.65) results in a share value of 74%. Therefore, the share value of 74% was used for the lower limit, and the 95% calculated by the pharmaceutical company was used for the upper limit.

In addition, step 6 of the pharmaceutical company to determine the patients tested for the gBRCA-mutation was not included in the new calculation, as a test rate generally cannot be estimated here, since the SHI target population also includes patients whose existing gBRCA1/2-mutation has not yet been detected.

Further uncertainties remain as only the incidence of the disease was used, and prevalent patients as a whole were not considered.

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 Lynparza (active ingredient: olaparib) at the following publicly accessible link (last access: 15 May 2021)
https://www.ema.europa.eu/documents/product-information/lynparza-epar-product-information_de.pdf

Treatment with olaparib should only be initiated and monitored by specialists in internal medicine, haematology, and oncology and specialists participating in the Oncology Agreement who are experienced in the treatment of patients with adenocarcinoma of the pancreas.

2.4 Treatment costs

The treatment costs are based on the information of the product information as well as the information in the Lauer-Taxe (status: 15 May 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 patient-individual and/or is shorter on average. The time unit “days” is used to calculate the “number of treatments/patient/year”, time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

Treatment duration:

2 Hermann S, Kraywinkel K. Epidemiology of pancreatic cancer in Germany. The Oncologist 2019; 25(8): 647-652

Name of therapy	Treatment mode	Number of treatments/patient/year	Treatment duration/ treatment (days)	Days of treatment/ patient/ year
Medicinal product to be assessed				
Olaparib	continuously, twice a day	365	1	365
Appropriate comparator therapy				
Monitoring wait-and-see approach	incalculable			

Consumption:

Name of therapy	Dosage/ Application	Dosage/ patient/ days of treatment	Usage by strength/day of treatment	Days of treatment/ Patient/ Year	Average annual consumption by potency
Medicinal product to be assessed					
Olaparib	300 mg	600 mg	4 x 150 mg	365	1,460 x 150 mg
Appropriate comparator therapy					
Monitoring wait-and-see approach	incalculable				

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. For the calculation of the annual treatment costs, the required number of packs by strength was first determined on the basis of consumption. Having determined the number of packs of a particular strength, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates.

Cost of medicinal product:

Name of therapy	Package size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate § 130a SGB V	Cost after deduction of statutory rebates
Medicinal product to be assessed					
Olaparib	112 FCT	€ 5,616.98	€ 1,77	€ 317,51	€ 5,297,70
Appropriate comparator therapy					
Monitoring wait-and-see approach	incalculable				
Abbreviations: FCT = Film-coated tablets					

Stand Lauer-Taxe: 15 May 2021

Costs for additionally required SHI services:

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

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

As there are no regular differences in the necessary use of medical treatment or in the prescription of other services when using the medicinal product to be evaluated and the appropriate comparator therapy according to the product information, no costs for additionally required SHI services had to be considered.

3. Bureaucratic cost calculation

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

4. Process sequence

At its session on 27 November 2018, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 30 November 2020, the pharmaceutical company submitted a dossier for the benefit assessment of olaparib to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 2, sentence 2 VerfO.

By letter dated 2 December 2020 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefits of medicinal products

with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient olaparib.

The dossier assessment by the IQWiG was submitted to the G-BA on 11 March 2021, and the written statement procedure was initiated with publication on the G-BA website on 15 March 2021. The deadline for submitting written statements was 6 April 2021.

The oral hearing was held on 26 April 2021.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (WG 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 26 May 2021, and the draft resolution was approved.

At its session on 3 June 2021, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal product	27 November 2018	Implementation of the appropriate comparator therapy
Working group Section 35a	20 April 2021	Information on written statement procedures received; preparation of the oral hearing
Subcommittee Medicinal product	26 April 2021	Conduct of the oral hearing
Working group Section 35a	4 May 2021 18 May 2021	Consultation on the dossier assessment by the IQWiG, evaluation of the written statement procedure
Subcommittee Medicinal product	26 May 2021	Final discussion of the draft resolution
Plenum	3 June 2021	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 3 June 2021

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

Prof. Hecken