

Justification

of the Resolution of the Federal Joint Committee (G-BA) on
an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with
New Active Ingredients according to Section 35a (SGB V)
Durvalumab (new therapeutic indication:
hepatocellular carcinoma, first-line, monotherapy)

of 6 June 2024

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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 placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirements for a quality-assured application.

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

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

2. Key points of the resolution

The active ingredient durvalumab (Imfinzi) was listed for the first time on 15 October 2018 in the "LAUER-TAXE[®]", the extensive German registry of available drugs and their prices.

On 15 November 2023, durvalumab received marketing authorisation for a new therapeutic indication to be classified as a major type 2 variation 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 variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, sentence 7).

On 13 December 2023, the pharmaceutical company has submitted a dossier in accordance with Section 4, paragraph 3, number 2 Ordinance on 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 durvalumab with the

new therapeutic indication "for the first line treatment of advanced or unresectable hepatocellular carcinoma (HCC)" in due time (i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication).

The G-BA commissioned the IQWiG to carry out the dossier assessment. The benefit assessment was published on 15 March 2024 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of durvalumab compared to 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 evaluated 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 durvalumab.

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 Durvalumab (Imfinzi) in accordance with the product information

IMFINZI as monotherapy is indicated for the first line treatment of adults with advanced or unresectable hepatocellular carcinoma (HCC).

Therapeutic indication of the resolution (resolution of 6 June 2024):

see the approved therapeutic indication

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

- a) Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh A or no liver cirrhosis; first-line therapy

Appropriate comparator therapy for durvalumab as monotherapy:

- atezolizumab in combination with bevacizumab
- or*
- durvalumab in combination with tremelimumab

1 General Methods, version 7.0 from 19.09.2023. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

b) Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh B; first-line therapy

Appropriate comparator therapy for durvalumab as monotherapy:

- Best supportive care

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 paragraph 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):

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 G-BA 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.

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if it determines by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

1. for the first time, a medicinal product approved in the therapeutic indication is available with the medicinal product to be assessed,
2. according to the generally recognised state of medical knowledge, the off-label use is generally preferable to the medicinal products previously approved in the therapeutic indication, or
3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved in the therapeutic indication.

An appropriate comparator therapy may also be non-medicinal therapy, the best possible add-on therapy including symptomatic or palliative treatment, or monitoring wait-and-see approach.

Justification based on the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO and Section 6, paragraph 2 AM-NutzenV:

- on 1. In addition to durvalumab, medicinal products with the following active ingredients are approved in the therapeutic indication: atezolizumab, bevacizumab, lenvatinib, mitomycin, sorafenib and tremelimumab
- on 2. A non-medicinal therapy cannot be considered as an appropriate comparator therapy. For the present therapeutic indication, it is assumed that both curative treatment (corresponding to BCLC stages 0 and A) and locoregional therapy in BCLC stage B, in particular transarterial (chemo)embolisation (TACE or TAE), are not (no longer) considered.
- on 3. Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V:
 - Lenvatinib: Resolution of 22 March 2019
 - Atezolizumab: Resolution of 20 May 2021
 - Durvalumab: Resolution of 5 October 2023
 - Tremelimumab: Resolution of 5 October 2023

Annex VI to Section K of the Pharmaceuticals Directive – Active ingredients that cannot be prescribed in applications beyond the scope of the marketing authorisation (off-label use):

- octreotide in hepatocellular carcinoma
- on 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V".

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present therapeutic indication according to Section 35a, paragraph 7 SGB V.

Among the approved active ingredients listed under 1., only certain active ingredients named below will be included in the appropriate comparator therapy, taking into account the evidence on therapeutic benefit, the guideline recommendations and the reality of care.

For use as first-line therapy, it is assumed that both curative treatment (corresponding to BCLC stages 0 and A) and locoregional therapy in BCLC stage B, in particular transarterial (chemo)embolisation (TACE or TAE), are not (no longer) considered.

It is also assumed that patients with BCLC stage D are ineligible for therapy with durvalumab.

According to the available guidelines, the stage of the disease and the functional capacity of the liver mainly determine the treatment decision for first-line treatment of hepatocellular carcinoma. Against this background, it is considered appropriate to

differentiate the determination of the appropriate comparator therapy according to the following patient groups:

a) Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh A or no liver cirrhosis; first-line therapy

According to the generally accepted state of medical knowledge, patients with hepatocellular carcinoma in stage BCLC B or C and with preserved liver function (Child-Pugh score A) are eligible for systemic therapy. Furthermore, according to the available evidence, a change has taken place in the mentioned patient group or treatment setting with regard to the therapy standard.

Several substances are available for the treatment of advanced HCC. For first-line therapy, these include the combination therapies atezolizumab + bevacizumab and durvalumab + tremelimumab and monotherapies with durvalumab as well as with the tyrosine kinase inhibitors sorafenib or lenvatinib.

According to the current S3 guideline,² the relevant patients should be offered first-line therapy with atezolizumab in combination with bevacizumab or with durvalumab in combination with tremelimumab. According to the recommendations of the guidelines, both combination therapies are equally recommended first-choice therapy options. According to the guidelines, the therapy options lenvatinib or sorafenib only assume significance as alternatives to first-line therapy in patients with a contraindication to atezolizumab + bevacizumab or durvalumab + tremelimumab.

In their written statement, the scientific-medical societies cite the combination therapies atezolizumab + bevacizumab and durvalumab + tremelimumab as the current therapy standard.

By resolution of 22 March 2019, the G-BA had not identified any additional benefit of lenvatinib over sorafenib in the benefit assessment for patients with Child-Pugh A or no liver cirrhosis without prior systemic therapy.

By resolution of 20 May 2021, the G-BA identified an indication of a considerable additional benefit over sorafenib in the benefit assessment of atezolizumab in combination with bevacizumab in patients with Child-Pugh A or no liver cirrhosis who have not received prior systemic treatment.

No additional benefit was identified for the combination therapy durvalumab and tremelimumab for patients with Child-Pugh A or no liver cirrhosis in first-line treatment on the basis of an adjusted indirect comparison with atezolizumab in combination with bevacizumab via the bridge comparator sorafenib (resolutions of 5 October 2023).

In the overall analysis, according to the generally recognised state of medical knowledge, first-line treatment with atezolizumab in combination with bevacizumab or durvalumab in combination with tremelimumab represents the current therapy standard for patients with Child-Pugh A or no liver cirrhosis and is determined to be the appropriate comparator therapy.

² German Society for Gastroenterology, Digestive and Metabolic Diseases (DGVS), August 2023. Association of the Scientific-Medical Societies (AWMF); Diagnosis and treatment of hepatocellular carcinoma and biliary carcinoma; S3 guideline, long version 4.0

The appropriate comparator therapy determined here includes several therapy options. These therapeutic alternatives are equally appropriate for the comparator therapy.

The additional benefit can be proven compared to one of the therapeutic alternatives mentioned; usually, this can be done within the framework of a single-comparator study.

b) Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh B; first-line therapy

According to the generally accepted state of medical knowledge, antineoplastic systemic therapy is generally only recommended for patients in Child-Pugh score A. In the guidelines, it is recommended offering systemic therapy with sorafenib or with an anti-PD-1 antibody (nivolumab/ pembrolizumab) also in Child-Pugh score B (up to 8 points) only in individual cases. This recommendation is only an open recommendation (recommendation grade 0) for both therapy options. In addition, anti-PD-1 antibodies are not approved in the therapeutic indication. Sorafenib and anti-PD-1 antibodies are therefore not considered as appropriate comparator therapy.

Best supportive care for patients with Child-Pugh score B is determined as the appropriate comparator therapy. Best supportive care is the therapy that provides the best possible, patient-individually optimised supportive treatment to alleviate symptoms and improve quality of life.

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

A change in the appropriate comparator therapy requires a resolution by the G-BA linked to the prior review of the criteria according to Chapter 5 Section 6, paragraph 3 Rules of Procedure.

Change of the appropriate comparator therapy:

Originally, the appropriate comparator therapy for patient group a) was determined as follows:

Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh A or no liver cirrhosis; first-line therapy

Appropriate comparator therapy for durvalumab (monotherapy):

- atezolizumab in combination with bevacizumab

From the written statement in the written statement procedure of the present benefit assessment on the question of the therapy currently used in clinical practice, it emerged from the assessment of the scientific-medical societies that both combination therapies atezolizumab in combination with bevacizumab and durvalumab in combination with tremelimumab are the current therapy standard in clinical practice. This is also reflected in the recommendations of the current guidelines. Due to the further development of the state of medical knowledge, the combination therapy durvalumab in combination with

tremelimumab is added as an alternative comparator therapy for patient group a) for the present resolution.

The present resolution is limited in time, which enables the pharmaceutical company to submit suitable evaluations in a new dossier for comparison with the appropriate comparator therapy specified in the present resolution.

2.1.3 Extent and probability of the additional benefit

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

a) Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh A or no liver cirrhosis; first-line therapy

An additional benefit is not proven.

Justification:

For the proof of additional benefit of durvalumab as monotherapy compared with the appropriate comparator therapy atezolizumab + bevacizumab, the pharmaceutical company used an adjusted indirect comparison according to the procedure by Bucher et al. For the adjusted indirect comparison via the bridge comparator of sorafenib, the pharmaceutical company includes the HIMALAYA study on the side of durvalumab and the IMbrave150 study on the side of atezolizumab + bevacizumab.

Description of the HIMALAYA study

The HIMALAYA study is an open-label randomised controlled trial comparing durvalumab as monotherapy or durvalumab in combination with tremelimumab versus sorafenib with 4 treatment arms. For the present benefit assessment, the comparison of durvalumab as monotherapy versus sorafenib is used. The study ongoing since 2017 is being conducted in 170 study sites in North and South America, Europe and Asia.

Adults with advanced or unresectable HCC who are ineligible for locoregional therapy and had not received prior systemic therapy for HCC were enrolled in the study. Further requirements for enrolment in the study were a Barcelona Clinic Liver Cancer (BCLC) stage B or C, as well as a Child-Pugh score A and an Eastern Cooperative Oncology Group - Performance Status (ECOG-PS) of 0 or 1.

A total of 778 patients were allocated to the durvalumab (monotherapy) (389 patients) and sorafenib (389 patients) study arms. In terms of aetiology, around 31% of patients had a hepatitis B infection, around 27% a hepatitis C infection and around 42% non-viral aetiology as the cause of HCC.

The primary endpoint of the study was overall survival. Patient-relevant secondary endpoints were morbidity, health-related quality of life, and adverse events (AEs).

For the HIMALAYA study, 4 data cut-offs are available in total:

- 1st data cut-off from 02.09.2019: interim analysis for objective response rate and duration of response

- 2nd data cut-off from 22.05.2020: interim analysis for overall survival
- 3rd data cut-off from 27.08.2021: final analysis of overall survival
- 4th data cut-off from 23.01.2023: exploratory long-term follow-up data on overall survival and SAE

For the endpoints of overall survival and SAE, analyses on the 3rd data cut-off from 27 August 2021 and on the 4th data cut-off from 23.01.2023 were presented in the dossier. As the 4th data cut-off from 23.01.2023 was not pre-specified (specification in protocol version 7 of 22.09.2021 after the final analysis of overall survival), the results of the 4th data cut-off were not used for the benefit assessment. The 3rd data cut-off from 27.08.2021 is used for the benefit assessment.

Description of the IMbrave150 study

The IMbrave 150 study is an open-label, randomised controlled phase III study conducted in 111 study sites in Asia, Australia, Europe and North America from 2018 to 2022.

Adult patients with locally advanced or metastatic and/or unresectable HCC who have not previously received systemic therapy were enrolled in the study. Further requirement for enrolment in the study were a Child-Pugh score A classification and a general condition according to ECOG-PS of 0 or 1.

A total of 558 patients were randomised in a 2:1 ratio to treatment with atezolizumab + bevacizumab (N = 375) or sorafenib (N = 183). In terms of aetiology, around 50% of patients had a hepatitis B infection, around 20% a hepatitis C infection and around 29% non-viral aetiology as the cause of HCC.

Co-primary endpoints in the study were overall survival and progression-free survival. Patient-relevant secondary endpoints were morbidity, health-related quality of life, and adverse events.

For the IMbrave150 study, 3 data cut-offs are available in total:

- 1st data cut-off from 29.08.2019: primary analysis of PFS and final analysis of overall survival
- 2nd data cut-off from 29.11.2019: 3-month safety update of the Food and Drug Administration (FDA): only evaluations of AEs
- 3rd data cut-off from 31.08.2020: analysis of overall survival and PFS, among other things, as part of the marketing authorisation at the request of the European Medicines Agency (EMA)

The pharmaceutical company submits evaluations for the endpoint of overall survival for the most recent data cut-off from 31.08.2020. For the endpoints of the category morbidity and health-related quality of life, results are available for the 1st data cut-off, which are not presented by the pharmaceutical company in the dossier. The analysis of AE endpoints is based on the most recent data cut-offs from 29.11.2019 (total population) and 29.08.2019 (Chinese cohort).

For indirect comparison

A core requirement for the consideration of studies in the adjusted indirect comparison via a bridge comparator is similarity.

In terms of study design, patient population and bridge comparator, the HIMALAYA and IMbrave150 studies are similar.

With regard to the similarity of the patient populations of the HIMALAYA and IMbrave150 studies, the demographic and clinical characteristics are sufficiently comparable. Differences are seen in the percentages of patients affected by macrovascular invasion and/or extrahepatic spread (HIMALAYA study approx. 65% vs IMbrave150 study approx. 76%). This is negligible as no relevant effect modifications are known for this characteristic. Larger differences between the two study populations are shown with regard to the aetiology of HCC, a known effect modifier, by infection with hepatitis B (IMbrave150 study approx. 50% vs HIMALAYA study approx. 31%) or non-viral aetiology (IMbrave150 study approx. 29% vs HIMALAYA study approx. 42%). These differences are also partly reflected in different percentages of the Asian region in the studies (HIMALAYA study approx. 42% vs IMbrave150 study 46%).

The planned observation of the endpoints on morbidity, health-related quality of life and severe AEs differs between the studies. In the present assessment, these differences in the planned duration of follow-up have no consequences for the morbidity endpoints, as there are no suitable data for the indirect comparison regardless of this.

There are differences between the sorafenib arms of the HIMALAYA and IMbrave150 studies (1st data cut-off), both for the median treatment duration (4.1 months vs 2.8 months) and for the median duration of observation for the endpoint of overall survival (13.3 months vs 10.4 months). No data are available for the treatment duration of patients in the IMbrave150 study at the 2nd data cut-off (31.08.2020), therefore it remains unclear whether the differences will also persist at this data cut-off. It is unclear how the durations of observation for overall survival were calculated or estimated. Sufficient similarity of the durations of observation is assumed as the actually observed median survival times for the endpoint of overall survival do not differ between the studies (13.8 vs 13.4 months).

In summary, there are partial differences in study and patient characteristics between the HIMALAYA and IMbrave150 studies, none of which, however, fundamentally calls into question the sufficient similarity to conduct an adjusted indirect comparison via the bridge comparator sorafenib.

Aetiology of HCC and subgroup analyses

There are differences in the viral aetiology of HCC between the regions of Asia and Africa (higher percentage of hepatitis B infections) and Japan, North America and Western Europe (higher percentage of hepatitis C infections). In Germany, non-viral (including high alcohol consumption and metabolic causes) aetiologies and hepatitis C infections are the main cause of liver tumours. There are therefore differences in the distribution of the aetiological characteristic between the patients in the study population and the patients in the German healthcare context.

In the dossier, the pharmaceutical company does not submit any subgroup analyses for the indirect comparison. In the benefit assessment of atezolizumab + bevacizumab, subgroup

analyses for the aetiology characteristic of HCC (hepatitis B or C vs non-viral aetiology) showed an effect modification in overall survival to the advantage of patients with viral aetiology of HCC. Based on the present data constellation, data in this regard would have been desirable. The pharmaceutical company only presented subgroup analyses in this regard on the basis of a non-pre-specified data cut-off of the HIMALAYA study (data cut-off from 23.01.2023), which is not used for the benefit assessment. These analyses showed non-significant interaction tests. Due to the lack of subgroup analyses for the indirect comparison, no statements can be made about potential effect modifications for the comparison of durvalumab and atezolizumab + bevacizumab.

Extent and probability of the additional benefit

Mortality

For the endpoint of overall survival, the adjusted indirect comparison does not show any statistically significant difference between durvalumab (monotherapy) and atezolizumab + bevacizumab. For overall survival, an additional benefit of durvalumab compared to atezolizumab + bevacizumab is therefore not proven.

Morbidity and quality of life

For the endpoints of the categories of morbidity and quality of life, no suitable data are available for an indirect comparison.

There are differences in the observation durations in both HIMALAYA and IMbrave150 studies. Therefore, in the present situation, evaluations on time to first deterioration are to be used. However, such analyses are only available for the IMbrave150 study. Furthermore, there is a high risk of bias for all of the endpoints mentioned for morbidity and health-related quality of life, at least due to the lack of blinding in the subjective endpoint collection, so that the requirement for reliability of data for the implementation of an adjusted indirect comparison would not be fulfilled.

Side effects

Adverse events (AEs) in total

AEs occurred in 88.9% of patients in the HIMALAYA study and in 95.5% of patients in the IMbrave150 study. The results for the endpoint "total adverse events" are only presented additionally.

Serious adverse events (SAE)

For the endpoint of SAEs, the adjusted indirect comparison does not show any statistically significant difference between durvalumab (monotherapy) compared to atezolizumab + bevacizumab.

Severe AEs (CTCAE grade ≥ 3), discontinuation due to AEs

There is a systematically different duration of observation for severe AEs in both studies. This results in uncertainties in the interpretation of the results from the indirect comparison for the endpoint of severe AEs.

For the endpoint of discontinuation due to AEs, the open-label study design leads to a high risk of bias.

Due to the low reliability of data, the requirements for an indirect comparison are not met.

PRO-CTCAE, immune-mediated AEs and bleeding

The endpoints of PRO-CTCAE and bleeding were collected in the HIMALAYA and/or IMbrave150 studies, but no data on the endpoint were presented in the dossier.

For the endpoint of immune-mediated AEs, a review of the comparability of the operationalisations of immune-mediated AEs between the studies is lacking.

The data for the 3rd data cut-off of the HIMALAYA study subsequently submitted by the pharmaceutical manufacturer in the written statement procedure for immune-mediated AEs and bleeding events are unsuitable for the benefit assessment, as information on the comparability of the operationalisations between the studies is still missing. In addition, no suitable data are available for the IMbrave150 study due to the lack of a summary analysis of immune-mediated AEs, among other reasons. For the endpoint of immune-mediated AEs, no indirect comparison is performed in the present assessment.

No suitable data or none at all are available for the endpoints of PRO-CTCAE, bleeding and immune-mediated AEs.

Overall, there is neither an advantage nor disadvantage of durvalumab compared to atezolizumab + bevacizumab in terms of side effects.

Overall assessment

For the assessment of the additional benefit of durvalumab (monotherapy) versus atezolizumab in combination with bevacizumab in adults with advanced or unresectable HCC with Child-Pugh A or no liver cirrhosis, results are available from the adjusted indirect comparison of the HIMALAYA study with the IMbrave150 study via the bridge comparator sorafenib. The studies presented are sufficiently similar and overall suitable for conducting an adjusted indirect comparison.

There was no statistically significant difference for the endpoint of overall survival.

The data on morbidity and quality of life collected in the individual studies are unsuitable for the adjusted indirect comparison.

Overall, there is neither an advantage nor disadvantage of durvalumab compared to atezolizumab + bevacizumab in terms of side effects. There are uncertainties in the interpretation of the results for the endpoint of severe AEs. No suitable data are available for the endpoint of discontinuation due to AEs.

In the overall assessment, an additional benefit of durvalumab (monotherapy) over atezolizumab in combination with bevacizumab in adults with advanced or unresectable HCC with Child-Pugh A or no liver cirrhosis is not proven.

b) Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh B; first-line therapy

An additional benefit is not proven.

Justification:

For adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh B in first-line therapy, the pharmaceutical company does not submit data for the assessment of additional benefit. Therefore, an additional benefit is not proven.

2.1.4 Limitation of the period of validity of the resolution

The limitation of the period of validity of the resolution on the present benefit assessment of durvalumab finds its legal basis in Section 35a paragraph 3 sentence 5 SGB V. Thereafter, the G-BA may limit the validity of the resolution on the benefit assessment of a medicinal product. In the present case, the limitation is justified by objective reasons consistent with the purpose of the benefit assessment pursuant to Section 35a paragraph 1 SGB V.

Due to the present change in the appropriate comparator therapy, the G-BA considers it appropriate to limit the resolution on the additional benefit of durvalumab. The limitation enables the pharmaceutical company to submit suitable evaluations, which correspond to the appropriate comparator therapy determined by the present resolution, in a new dossier in a timely manner. For this purpose, a limitation of the period of validity of the resolution to 6 months is considered to be appropriate.

In accordance with Section 3 paragraph 1, number 5 AM-NutzenV in conjunction with Chapter 5 Section 1, paragraph 2, number 7 VerfO, the procedure for the benefit assessment of the medicinal product with the active ingredient durvalumab recommences when the deadline has expired. For this purpose, the pharmaceutical company must submit a dossier to the G-BA at the latest on the date of expiry to prove the extent of the additional benefit of durvalumab (Section 4, paragraph 3, number 5 AM-NutzenV in conjunction with Chapter 5 Section 8, paragraph 1, number 5 VerfO). If the dossier is not submitted or is incomplete, the G-BA may determine that an additional benefit is considered as being not proven. The possibility that a benefit assessment for the medicinal product with the active ingredient durvalumab can be carried out at an earlier point in time due to other reasons (cf. Chapter 5, Section 1 paragraph 2, Nos. 2 to 6 or No. 8 VerfO) remains unaffected hereof.

A new assessment according to Section 3, paragraph 1, No. 5 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 1, paragraph 2, No. 7 Rules of the Procedure (VerfO) will not take place if the pharmaceutical company does not wish to make use of the option to submit suitable evaluations corresponding to the appropriate comparator therapy specified in this resolution and irrevocably applies in writing to the G-BA for the resolution to be cancelled within 3 months of this resolution coming into force. In the event of a timely application for cancellation of the time limit, the G-BA shall cancel the limitation on the validity of this resolution with the consequence that the findings of this resolution shall then continue to apply beyond the end of the time limit.

2.1.5 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the medicinal product Imfinzi with the active ingredient durvalumab.

The therapeutic indication assessed here is as follows:

"IMFINZI as monotherapy is indicated for the first line treatment of adults with advanced or unresectable hepatocellular carcinoma (HCC)."

In the therapeutic indication under consideration, 2 patient groups were distinguished and the appropriate comparator therapy was determined as follows:

- a) Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh A or no liver cirrhosis; first-line therapy

Appropriate comparator therapy for durvalumab as monotherapy:

– atezolizumab in combination with bevacizumab

or

– durvalumab in combination with tremelimumab

- b) Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh B; first-line therapy

Appropriate comparator therapy for durvalumab as monotherapy:

– Best supportive care

Patient group a)

The pharmaceutical company presents an adjusted indirect comparison of durvalumab (HIMALAYA study) versus atezolizumab in combination with bevacizumab (IMbrave150 study) via the bridge comparator sorafenib for assessment. The studies presented are sufficiently similar and suitable for conducting an adjusted indirect comparison.

There is no relevant difference for the assessment of overall survival.

No suitable data are available for morbidity and quality of life.

Overall, there is neither an advantage nor disadvantage of durvalumab compared to atezolizumab + bevacizumab in terms of side effects. There are uncertainties in the interpretation of the results for the endpoints of severe AEs and discontinuation due to AEs.

In the overall assessment, an additional benefit of durvalumab (monotherapy) over atezolizumab in combination with bevacizumab in adults with advanced or unresectable HCC with Child-Pugh A or no liver cirrhosis is not proven.

The present resolution is limited in time until 1 January 2025, which enables the pharmaceutical company to submit evaluations relating to the appropriate comparator therapy amended by the present resolution.

Patient group b)

For adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh B in first-line therapy, the pharmaceutical company does not submit data for the assessment of additional benefit. Therefore, an additional benefit is not proven.

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 dossier submitted by the pharmaceutical company is fraught with uncertainties regarding the patient numbers due to the currently lower percentage of HCC in all liver tumours and a lower limit for patients with BCLC stage B HCC disease. In order to ensure a consistent determination of the patient numbers in the present therapeutic indication, the G-BA refers to the derivation of the target population used as a basis in the resolution on the benefit assessment of atezolizumab in combination with bevacizumab (resolution of 20 May 2021). Based on a current incidence in the year under review 2023 (in this case 10,527 vs 9,394 patients in the benefit assessment procedure for atezolizumab in combination with bevacizumab), the following patient numbers result: approx. 1,440 to 4,150 patients for patient group a) with Child-Pugh A or no liver cirrhosis, and approx. 460 to 1,320 patients for patient group b) with Child-Pugh B.

The resolution on atezolizumab in combination with bevacizumab (resolution of 20 May 2021) includes a more valid derivation of the patient numbers in the SHI target population, which can be used despite existing uncertainties.

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 Imfinzi (active ingredient: durvalumab) at the following publicly accessible link (last access: 28 May 2024):

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

Treatment with durvalumab should only be initiated and monitored by specialists in internal medicine, haematology and oncology as well as specialists in gastroenterology and other specialists participating in the Oncology Agreement, all of whom are experienced in the treatment of patients with hepatocellular carcinoma.

2.4 Treatment costs

The treatment costs are based on the requirements in the product information and the information listed in the LAUER-TAXE® (last revised: 1 May 2024).

The costs for the first year of treatment are shown for the cost representation in the resolution.

Treatment period:

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration varies from patient to patient 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 the maximum treatment duration, if specified in the product information.

In combination with durvalumab, tremelimumab is used as a single dose only on the first day of the first cycle, followed by durvalumab monotherapy every 4 weeks.

a) Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh A or no liver cirrhosis; first-line therapy

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Durvalumab	1 x every 28 days	13.0	1	13.0
Appropriate comparator therapy				
<i>atezolizumab + bevacizumab</i>				
Atezolizumab	1 x every 14 days	26.1	1	26.1
	<i>or</i>			
	1 x every 21 days	17.4	1	17.4
	<i>or</i>			
	1 x every 28 days	13.0	1	13.0
Bevacizumab	1 x every 21 days	17.4	1	17.4
<i>Durvalumab + tremelimumab</i>				
Durvalumab	1 x every 28 days	13	1	13.0
Tremelimumab	Single dose on day 1 in cycle 1	1	1	1.0

b) Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh B; first-line therapy

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Durvalumab	1 x every 28 days	13.0	1	13.0
Best supportive care	Different from patient to patient			
Appropriate comparator therapy				

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Best supportive care	Different from patient to patient			

Consumption:

For the calculation of dosages depending on body weight (BW), the average body measurements from the official representative statistics “Microcensus 2021 – body measurements of the population” were applied (average body weight: 77.7 kg).³

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or comorbidities) are not taken into account when calculating the annual treatment costs.

Weight-based durvalumab dosage is required for patients weighing 30 kg or less – durvalumab 10 mg/kg every 2 weeks or 20 mg/kg every 4 weeks as monotherapy until body weight has increased to over 30 kg.

The treatment costs for best supportive care are different from patient to patient. Because best supportive care has been determined as an appropriate comparator therapy, this is also reflected in the medicinal product to be assessed. The type and scope of best supportive care can vary depending on the medicinal product to be assessed and the comparator therapy.

a) Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh A or no liver cirrhosis; first-line therapy

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Durvalumab	1,500 mg	1,500 mg	3 x 500 mg	13.0	39.0 x 500 mg
Appropriate comparator therapy					
<i>atezolizumab + bevacizumab</i>					
Atezolizumab	840 mg	840 mg	1 x 840 mg	26.1	26.1 x 840 mg
	<i>or</i>				
	1,200 mg	1,200 mg	1 x 1,200 mg	17.4	17.4 x 1,200 mg

³ Federal Statistical Office, Wiesbaden 2018: <http://www.gbe-bund.de/>

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	<i>or</i>				
	1,680 mg	1,680 mg	2 x 840 mg	13.0	26.0 x 840 mg
Bevacizumab	15 mg/ kg BW = 1,165.5 mg	1,165.5 mg	3 x 400 mg	17.4	52.2 x 400 mg
<i>Durvalumab + tremelimumab</i>					
Durvalumab	1,500 mg	1,500 mg	3 x 500 mg	13.0	39.0 x 500 mg
Tremelimumab	300 mg	300 mg	1 x 300 mg	1.0	1 x 300 mg

b) Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh B; first-line therapy

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient / year	Average annual consumption by potency
Medicinal product to be assessed					
Durvalumab	1,500 mg	1,500 mg	3 x 500 mg	13.0	39 x 500 mg
Best supportive care ⁴	Different from patient to patient				
Appropriate comparator therapy					
Best supportive care ⁴	Different from patient to patient				

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 Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis

⁴ When comparing durvalumab with best supportive care, the costs of best supportive care must also be additionally considered for the medicinal product to be assessed.

of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. Any fixed reimbursement rates shown in the cost representation may not represent the cheapest available alternative.

Costs of the medicinal products:

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Durvalumab 500 mg	1 CIS	€ 2,167.38	€ 2.00	€ 120.49	€ 2,044.89
Appropriate comparator therapy					
Atezolizumab 840 mg	1 CIS	€ 2,907.75	€ 2.00	€ 162.77	€ 2,742.98
Atezolizumab 1,200 mg	1 CIS	€ 4,129.23	€ 2.00	€ 232.53	€ 3,894.70
Bevacizumab 25 mg/ml	1 CIS	€ 1,553.33	€ 2.00	€ 85.42	€ 1,465.91
Durvalumab 500 mg	1 CIS	€ 2,167.38	€ 2.00	€ 120.49	€ 2,044.89
Tremelimumab 300 mg	1 CIS	€ 27,320.89	€ 2.00	€ 1,557.01	€ 25,761.88
Abbreviations: CIS = concentrate for the preparation of an infusion solution					

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Costs for additionally required SHI services:

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

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

Because there are no regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, no costs for additionally required SHI services need to be taken into account.

Other SHI benefits:

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

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic agents a maximum amount of € 100 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 100 per ready-to-use unit are to be payable. These additional other costs do not add to the pharmacy sales price but follow the rules for calculation in the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe). The cost representation is based on the pharmacy retail price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

2.5 Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

According to Section 35a, paragraph 3, sentence 4, the G-BA designates all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is approved exclusively for use in monotherapy, a combination therapy is not considered due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA has decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c, sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA has decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d

SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

With regard to the further examination steps, a differentiation is made between a "determined" or "undetermined" combination, which may also be the basis for a designation.

A "determined combination" exists if one or more individual active ingredients which can be used in combination with the assessed medicinal product in the assessed therapeutic indication are specifically named.

An "undetermined combination" exists if there is information on a combination therapy, but no specific active ingredients are named. An undetermined combination may be present if the information on a combination therapy:

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or
- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more detail in the relevant product information, which, however, does not include information on active ingredients within the scope of this therapeutic indication.

Concomitant active ingredient

The concomitant active ingredient is a medicinal product with new active ingredients that can be used in combination therapy with the assessed medicinal product for the therapeutic indication to be assessed.

For a medicinal product to be considered as a concomitant active ingredient, it must be classified as a medicinal product with new active ingredients according to Section 2 paragraph 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with the corresponding regulations in Chapter 5 of the Rules of Procedure of the G-BA as of the date of the present resolution. In addition, the medicinal product must be approved in the assessed therapeutic indication, whereby a marketing authorisation is sufficient only for a sub-area of the assessed therapeutic indication.

Based on an "undetermined combination", the concomitant active ingredient must be attributable to the information on the product class or group or the therapeutic indication according to the product information of the assessed medicinal product in the assessed therapeutic indication, whereby the definition of a product class or group is based on the corresponding information in the product information of the assessed medicinal product.

In addition, there must be no reasons for exclusion of the concomitant active ingredient from a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic

indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

Medicinal products with new active ingredients for which the G-BA has decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients, provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

If the present resolution on the assessed medicinal product in the assessed therapeutic indication contains several patient groups, the designation of concomitant active ingredients shall be made separately for each of the patient groups.

Exception to the designation

The designation excludes combination therapies for which - patient group-related - a considerable or major additional benefit has been determined by resolution according to Section 35a, paragraph 3, sentence 1 SGB V or it has been determined according to Section 35a, paragraph 1d, sentence 1 SGB V that at least considerable additional benefit of the combination can be expected. In this context, the combination therapy that is excluded from the designation must, as a rule, be identical to the combination therapy on which the preceding findings were based.

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the

combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGB V.

The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

Justification for the findings on designation in the present resolution:

a) Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh A or no liver cirrhosis; first-line therapy

No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.

References:

Product information for durvalumab (Imfinzi); product information for IMFINZI® 50 mg/ml concentrate for the preparation of an infusion solution; last revised: February 2024

b) Adults with advanced or unresectable hepatocellular carcinoma (HCC) with Child-Pugh B; first-line therapy

No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.

References:

Product information for durvalumab (Imfinzi); product information for IMFINZI® 50 mg/ml concentrate for the preparation of an infusion solution; last revised: February 2024

3. Bureaucratic costs calculation

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

4. Process sequence

At its session on 25 January 2022, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 13 December 2023 the pharmaceutical company submitted a dossier for the benefit assessment of durvalumab to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 2 VerfO.

By letter dated 15 December 2023 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit 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 durvalumab.

The dossier assessment by the IQWiG was submitted to the G-BA on 11 March 2024, and the written statement procedure was initiated with publication on the G-BA website on 15 March 2024. The deadline for submitting statements was 5 April 2024.

The oral hearing was held on 22 April 2024.

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 was discussed at the session of the subcommittee on 28 May 2024, and the proposed resolution was approved.

At its session on 6 June 2024, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	25 January 2022	Implementation of the appropriate comparator therapy
Working group Section 35a	17 April 2024	Information on written statements received, preparation of the oral hearing
Subcommittee Medicinal products	22 April 2024	Conduct of the oral hearing
Working group Section 35a	30 April 2024 15 May 2024	Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure
Subcommittee Medicinal products	28 May 2024	Concluding discussion of the draft resolution

Plenum	6 June 2024	Adoption of the resolution on the amendment of the Pharmaceuticals Directive
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Berlin, 6 June 2024

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

Prof. Hecken