Gemeinsamer Bundesausschuss

# 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 Ribociclib (new therapeutic indication: breast cancer, HR+, HER2-, early at high risk of recurrence, adjuvant treatment, combination with aromatase inhibitor)

of 5 June 2025

**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 all 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 ribociclib (Kisqali) was listed for the first time on 15 September 2017 in the “LAUER-TAXE®”, the extensive German registry of available drugs and their prices.

On 25 November 2024, ribociclib 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 16 December 2024, i.e. at the latest within four weeks after informing the pharmaceutical company about the approval for a new therapeutic indication, the pharmaceutical company has submitted a dossier in due time 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 ribociclib with the new therapeutic indication

"Kisqali in combination with an aromatase inhibitor is indicated for the adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence.

In pre- or perimenopausal women, or in men, the aromatase inhibitor should be combined with a luteinising hormone-releasing hormone (LHRH) agonist."

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 17 March 2025 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 ribociclib 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, as well of the addendum drawn up by the IQWiG on the benefit assessment. 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 ribociclib.

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 Ribociclib (Kisqali) in accordance with the product information

Kisqali in combination with an aromatase inhibitor is indicated for the adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence.

In pre- or perimenopausal women, or in men, the aromatase inhibitor should be combined with a luteinising hormone-releasing hormone (LHRH) agonist.

**Therapeutic indication of the resolution (resolution of 5 June 2025):**

See the approved therapeutic indication.

### 2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

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

a1) Premenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

Appropriate comparator therapy for ribociclib in combination with an aromatase inhibitor:

- Tamoxifen (if necessary, in addition with cessation of ovarian function)

or

- abemaciclib in combination with endocrine therapy (only for female patients with node-positive breast cancer)

or

- olaparib as monotherapy or in combination with endocrine therapy (only for female patients with germline BRCA1/2-mutations)

or

- an aromatase inhibitor (anastrozole or letrozole or exemestane) in combination with cessation of ovarian function (exemestane only in combination with triptorelin)

a2) Postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

Appropriate comparator therapy for ribociclib in combination with an aromatase inhibitor:

- An aromatase inhibitor (anastrozole or letrozole) alone, or, if applicable, tamoxifen if aromatase inhibitors are unsuitable

or

- an aromatase inhibitor (anastrozole or exemestane) in sequence after tamoxifen

or

- olaparib as monotherapy or in combination with endocrine therapy (only for female patients with germline BRCA1/2-mutations)

a3) Men with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

Appropriate comparator therapy for ribociclib in combination with an aromatase inhibitor:

- Tamoxifen

or

- abemaciclib in combination with endocrine therapy (only for patients with node-positive breast cancer)

or

- Olaparib as monotherapy or in combination with endocrine therapy (only for male patients with germline BRCA1/2-mutations)

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 ribociclib, the active ingredients tamoxifen, anastrozole, exemestane, letrozole, leuprorelin, goserelin, triptorelin, cyclophosphamide, docetaxel, doxorubicin, epirubicin, fluorouracil, methotrexate, paclitaxel, vincristine, abemaciclib and olaparib are approved in the present therapeutic indication.

Medicinal products with explicit marketing authorisation for hormone receptor (HR)-negative breast cancer, HER2-positive breast cancer and advanced metastatic breast cancer are not considered.

On 2. In principle, radiotherapy, radiomenolysis and ovariectomy can be considered as non-medicinal treatments in this therapeutic indication.

Adjuvant radiotherapy has a high significance in the present therapeutic indication, especially in case of a high risk of recurrence. Adjuvant radiotherapy can be given sequentially or in parallel with endocrine therapy. It is assumed that the patients have received prior radiotherapy. An adjuvant radiotherapy is therefore not part of the appropriate comparator therapy.

On 3. In the therapeutic indication, the following resolutions from the G-BA on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V are available:

- Abemaciclib (in combination with endocrine therapy): resolution of 20 October 2022
- Olaparib (as monotherapy or in combination with endocrine therapy): resolution of 16 February 2023

In the therapeutic indication, the following resolutions or guidelines of the G-BA for medical or non-medicinal treatments are available:

Directive on Examination and Treatment Methods in Hospitals (Directive on Inpatient Treatment Methods) - Methods excluded from provision at the expense of the statutory health insurance funds:

- Proton therapy for breast cancer

Guideline for the regulation of requirements for disease management programmes (DMP) in accordance with Section 137f paragraph 2 SGB V (DMP Requirements Guideline), Annex 3 Requirements for the design of structured treatment programmes for female patients with breast cancer

Directive on methods of medical care provided by SHI-accredited physicians: Biomarker-based tests for deciding for or against adjuvant systemic chemotherapy in primary breast cancer

- Pharmaceuticals Directive, Annex VI (off-label use)

- Part A: XXXVII. Bisphosphonates in female patients with hormone receptor (HR)-positive, postmenopausal breast cancer: Adjuvant bisphosphonate therapy in female patients with hormone receptor (HR)-positive, postmenopausal breast cancer

- Part B: IV. Gemcitabine in monotherapy for breast cancer in women

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as reviews of clinical studies in the present therapeutic indication. 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. No corresponding written feedback was submitted.

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.

When determining the appropriate comparator therapy for the present therapeutic indication, it was assumed that adjuvant chemotherapy - if indicated - has been completed.

There are different recommendations for adjuvant endocrine therapy for pre- and postmenopausal women and for men.

*Premenopausal women*

In the adjuvant treatment of hormone receptor (HR)-positive breast cancer in premenopausal women, guidelines recommend tamoxifen, whereby additional cessation of ovarian function should be considered. Against the background that the present therapeutic indication explicitly includes female patients at a high risk of recurrence, it is stated that, in addition to tamoxifen, cessation of ovarian function is included in the appropriate comparator therapy, if applicable.

The active ingredient abemaciclib is also recommended in the guidelines. Abemaciclib is approved for the adjuvant treatment of HR-positive, HER-2 negative, node-positive early breast cancer at high risk of recurrence. In the benefit assessment, a hint for a minor additional benefit was identified for premenopausal women by resolution of 22 October 2022. The period of validity of this finding is limited to 1 July 2026. Abemaciclib in combination with endocrine therapy is also included in the appropriate comparator therapy in accordance with the marketing authorisation for female patients with node-positive breast cancer.

In addition, the active ingredient olaparib has been approved for the adjuvant treatment of adult patients with germline BRCA1/2-mutations who have HER2-negative early breast cancer at high risk of recurrence. An indication of a minor additional benefit over the monitoring wait-and-see approach was identified by resolution of 16 February 2023. In accordance with the marketing authorisation, olaparib is also included in the appropriate comparator therapy.

Furthermore, in addition to the combination with tamoxifen, the active ingredient triptorelin - a GnRH analogue - is approved in combination with an aromatase inhibitor for premenopausal women at high risk of recurrence. This marketing authorisation also includes the combination with exemestane. The aromatase inhibitors anastrozole and letrozole are also approved for initial endocrine therapy of postmenopausal women. According to the information provided by the Federal Institute for Drugs and Medical Devices (BfArM), the marketing authorisations for anastrozole and letrozole - with regard to premenopausal women - do not formally exclude female patients whose menopause has been surgically or medicinally induced (using LHRH agonists). In the statements by clinical experts in the present benefit assessment procedure, aromatase inhibitors in combination with cessation of ovarian function assume high significance in

the adjuvant treatment of premenopausal patients besides the other options mentioned above. Against this background, aromatase inhibitors (anastrozole or letrozole or exemestane) in combination with cessation of ovarian function are also determined to be an appropriate comparator therapy, whereby exemestane is only approved in combination with triptorelin.

*Postmenopausal women*

Aromatase inhibitors have a high significance in the adjuvant treatment of HR-positive breast cancer in postmenopausal women. There is a marketing authorisation for the two non-steroidal aromatase inhibitors anastrozole and letrozole for the treatment of postmenopausal women. The steroidal aromatase inhibitor exemestane is only approved after progression under anti-oestrogen treatment and is therefore not considered for initial adjuvant treatment as an appropriate comparator therapy. In case of intolerance to an aromatase inhibitor, tamoxifen is the recommended alternative for (further) adjuvant treatment.

In addition to sole treatment with an aromatase inhibitor (anastrozole or letrozole), or with tamoxifen if aromatase inhibitors are unsuitable, sequential treatment with initial tamoxifen followed by an aromatase inhibitor ("switch therapy") is another option. The aromatase inhibitors anastrozole and exemestane are approved for this purpose after 2-3 years of initial adjuvant treatment with tamoxifen. The aromatase inhibitor letrozole is approved 5 years after prior completed tamoxifen treatment ("extended adjuvant treatment"). This option with letrozole also has relatively weak evidence of benefit, especially considering IQWiG's report[2], and is also less strongly recommended in the guidelines. Therefore, sequential treatment with tamoxifen followed by letrozole is not included in the appropriate comparator therapy.

The active ingredient abemaciclib is also recommended in the guidelines. In the benefit assessment, it was determined by resolution of 22 October 2022 that an additional benefit is not proven for postmenopausal women. The period of validity of this finding is limited to 1 July 2026. Against this background, abemaciclib is not determined as an appropriate comparator therapy for postmenopausal women.

In addition, the active ingredient olaparib has been approved for the adjuvant treatment of adult patients with germline BRCA1/2-mutations who have HER2-negative early breast cancer at high risk of recurrence. By resolution of 16 February 2023, an indication of a minor additional benefit was identified. In accordance with the marketing authorisation, olaparib is also included in the appropriate comparator therapy.

Guidelines also recommend adjuvant bisphosphonate therapy for postmenopausal women. Bisphosphonates are not approved in this respect, but can be prescribed in accordance with Annex VI of the Pharmaceuticals Directive. In G-BA's opinion, adjuvant bisphosphonate therapy should be offered as an additional therapy to postmenopausal patients.

*Men*

[2] Institute for Quality and Efficiency in Health Care (IQWiG). Aromatase inhibitors in female breast cancer; final report; mandate A10-03. [online]. Cologne (GER): IQWiG; 2016. [Accessed: 22 April 2025]. (IQWiG reports; volume 437). URL: https://www.iqwig.de/download/A10-03_Abschlussbericht_Aromatasehemmer-beim-Mammakarzinom.pdf

Breast cancer in men is a very rare disease. The evidence on treatment options for men with breast cancer is accordingly extremely limited.

According to the guidelines, the recommendations for the treatment of men with breast cancer are predominantly based on the recommendations for the treatment of women. Aromatase inhibitors are only recommended for men with contraindications. The guidelines primarily recommend therapy with tamoxifen for men.

In addition, the active ingredient olaparib has been approved for the adjuvant treatment of adult patients with germline BRCA1/2-mutations who have HER2-negative early breast cancer at high risk of recurrence. By resolution of 16 February 2023, an indication of a minor additional benefit was identified. In accordance with the marketing authorisation, olaparib is also included in the appropriate comparator therapy.

The active ingredient abemaciclib is also approved for men. In the benefit assessment, it was determined by resolution of 22 October 2022 that an additional benefit is not proven for men. Against the background of the extremely limited evidence, abemaciclib is determined to be an appropriate comparator therapy for men.

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 a1) was determined as follows:

- "Tamoxifen (if necessary, in addition with cessation of ovarian function)

or

- abemaciclib in combination with endocrine therapy (only for female patients with node-positive breast cancer)

or

- olaparib as monotherapy or in combination with endocrine therapy (only for female patients with germline BRCA1/2-mutations)".

The adjustment of the appropriate comparator therapy with regard to the inclusion of aromatase inhibitors in combination with cessation of ovarian function takes particular account of the statements submitted by clinical experts in the present benefit assessment procedure on the significance of aromatase inhibitors in the adjuvant treatment of premenopausal women.

The change means that the results of the NATALEE study submitted by the pharmaceutical company in the dossier can be used for patient group a1). The corresponding results of the NATALEE study were analysed by IQWiG in the addendum to the dossier assessment. In addition, these results of the NATALEE study were the subject of the statements, which is why the change in the appropriate comparator therapy does not necessitate a renewed conduct of the benefit assessment procedure.

### 2.1.3 Extent and probability of the additional benefit

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

a1) Premenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

An additional benefit is not proven.

a2) Postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

An additional benefit is not proven.

a3) Men with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

An additional benefit is not proven.

Justification:

For the evidence of additional benefit, the pharmaceutical company has submitted in the dossier the results of the still ongoing, open-label, randomised controlled trial NATALEE, which compared ribociclib in combination with anastrozole or letrozole with anastrozole or letrozole.

Adult patients with HR-positive, HER2-negative early breast cancer at high risk of recurrence whose tumour had been completely resected were enrolled in the study.

A total of 5,101 patients were randomly assigned in a 1:1 ratio to treatment with ribociclib in combination with anastrozole or letrozole (intervention arm; N = 2,549) or anastrozole or letrozole (control arm; N = 2,552). Premenopausal women and men in both study arms also received a therapy with the GnRH analogue goserelin. Randomisation was stratified by menopausal status (premenopausal women and men vs postmenopausal women), tumour stage (II vs III), previous neoadjuvant/ adjuvant chemotherapy (yes vs no) and geographical region (North America/ Western Europe/ Oceania vs rest of the world).

Treatment with ribociclib was given for up to 36 months (approx. 39 cycles) or until recurrence, unacceptable toxicity, withdrawal of consent or death. Endocrine therapy with aromatase inhibitors was administered in both study arms up to a maximum of 60 months after randomisation or until one of the aforementioned events occurred. No limitations with regard to subsequent therapies existed.

The primary endpoint of the NATALEE study is invasive disease-free survival (iDFS). Patient-relevant endpoints are collected in the categories of mortality, morbidity, health-related quality of life and side effects.

Five data cut-offs are currently available for the NATALEE study, four of which were pre-specified (data cut-offs from 03.09.2021, 15.08.2022, 11.01.2023 and 21.07.2023). Another data cut-off from 29.04.2024, reported by the pharmaceutical company in the dossier, was

carried out at the request of a regulatory authority. This assessment is based on the results of the data cut-off from 29.04.2024.

Extent and probability of the additional benefit

a1) Premenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

Mortality

For the endpoint of overall survival, there was a statistically significant difference to the advantage of ribociclib in combination with an aromatase inhibitor compared to the control arm after a median duration of observation of approx. 44 months, based on low event numbers.

Although the extent of the achieved prolongation in overall survival is assessed as a relevant improvement, its extent is minimal.

Morbidity

*Recurrences (recurrence rate and invasive disease-free survival (iDFS)*

Patients in the present therapeutic indication are treated with a curative therapeutic approach. The failure of a curative therapeutic approach is fundamentally patient-relevant. The significance of the endpoints on recurrences depends on the extent to which the selected individual components are suitable for adequately reflecting the failure of potential cure by the present curative therapeutic approach.

In the present benefit assessment, both the recurrence rate and the evaluation as iDFS are considered for recurrences. Both evaluations include the following events:

- death due to any cause,
- local breast cancer recurrence,
- regional invasive breast cancer recurrence,
- contralateral invasive breast cancer,
- distant recurrence and
- secondary primary cancer (not breast cancer).

This operationalisation is considered suitable for depicting a failure of the potential cure through the curative therapeutic approach.

Both the event rate and the time-to-event analysis (iDFS) showed a statistically significant difference between ribociclib in combination with an aromatase inhibitor and the control arm over a median duration of observation of approx. 44 months. Although the extent of the achieved advantage in recurrences is assessed as a relevant improvement, its extent is minimal.

*Symptomatology (EORTC QLQ-C30 and EORTC QLQ-BR23)*

In the NATALEE study, patient-reported symptomatology was collected using the EORTC QLQ-C30 and EORTC QLQ-BR23.

There were statistically significant differences between the treatment arms in the fatigue, nausea and vomiting as well as constipation scales of the QLQ-C30 and the side effects of systemic therapy, chest symptoms and arm symptoms scales of the QLQ-BR23. However, the

95% confidence interval of the standardised mean difference (SMD) is not completely outside the irrelevance range of -0.2 to 0.2 in any of the scales. Thus, it cannot be inferred that the observed effects are relevant. There were no statistically significant differences in the other scales and no suitable data on burden due to hair loss scale of the QLQ-BR23 are available due to the lack of a sufficiently high percentage of analysable female patients.

*Health status (EQ-5D VAS)*

Data on patient-reported health status was collected in the NATALEE study using the EQ-5D visual analogue scale.

The results do not show any statistically significant difference between the treatment groups.

In summary, in the endpoint category of morbidity, there is an advantage of ribociclib in combination with an aromatase inhibitor in the avoidance of recurrences. There were no statistically significant or relevant differences with regard to patient-reported symptomatology or health status.

Quality of life

*EORTC QLQ-C30 and EORTC QLQ-BR23*

There were statistically significant differences between the treatment arms in the global health status scale as well as the physical functioning, role functioning and social functioning scales of the QLQ-C30. However, the 95% confidence interval of the standardised mean difference (SMD) is not completely outside the irrelevance range of -0.2 to 0.2 in any of the scales. Thus, it cannot be inferred that the observed effects are relevant.

There were no statistically significant differences in the other scales of QLQ-C30 and QLQ-BR23 and no suitable data on sexual pleasure scale of the QLQ-BR23 are available due to the lack of a sufficiently high percentage of analysable female patients.

Side effects

*Adverse events (AEs)*

In the NATALEE study, an adverse event occurred in 99% of female patients in the intervention arm and 90% thereof in the control arm. The results were only presented additionally.

*Serious adverse events (SAEs), severe adverse events (CTCAE grade ≥ 3) and discontinuation due to AEs*

For the endpoints of SAEs, severe AEs and discontinuation due to AEs, there was a statistically significant disadvantage of ribociclib in combination with an aromatase inhibitor compared to the control arm.

*Specific adverse events*

In detail, the specific AEs of Neutropenia (PT, severe AE), Skin and subcutaneous tissue disorders (SOC, AE), Respiratory, thoracic and mediastinal disorders (SOC, AE), Infections and infestations (SOC, severe AE), Gastrointestinal disorders (SOC, severe AE), General disorders and administration site conditions (SOC, severe AE) and hepatobiliary toxicity (SMQ, severe AE) each showed a statistically significant difference to the disadvantage of ribociclib in combination with an aromatase inhibitor.

In summary, due to the disadvantages in the endpoints of SAEs, severe AEs and discontinuation due to AEs, a significant disadvantage in side effects can be identified overall for treatment with ribociclib in combination with an aromatase inhibitor.

Overall assessment

For the endpoint categories of mortality, morbidity, health-related quality of life and side effects, results from the open-label, randomised, controlled and currently ongoing NATALEE study are available for the benefit assessment of ribociclib in combination with an aromatase inhibitor for adjuvant treatment of premenopausal patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence.

For the endpoint of overall survival, there was a statistically significant difference to the advantage of ribociclib in combination with an aromatase inhibitor compared to the control arm, based on low event numbers. Although the extent of the achieved prolongation in overall survival is assessed as a relevant improvement, its extent is minimal.

In the morbidity category, there was an advantage of ribociclib in combination with an aromatase inhibitor in the avoidance of recurrences. In the present curative treatment setting, the avoidance of recurrences is an essential therapeutic goal. There were no statistically significant or relevant differences with regard to patient-reported symptomatology or health status.

Likewise, there were no statistically significant or relevant differences in the health-related quality of life.

With regard to side effects, ribociclib in combination with an aromatase inhibitor showed statistically significant disadvantages for the endpoints of serious adverse events (SAEs), severe adverse events (AEs), discontinuation due to AEs and in detail also for specific AEs.

In the overall analysis, the advantages in terms of overall survival and recurrences are offset by significant disadvantages in terms of side effects. In a weighted decision, the G-BA came to the conclusion - against the background of the observed effect magnitude for overall survival and recurrences - that the significant disadvantages in terms of side effects challenge the advantages in terms of overall survival and recurrences. It is taken into account that the significance of the available results on overall survival and recurrences is limited, especially since censoring occurred early and then continuously over the entire course and to a relevant extent. It is therefore concluded that an additional benefit of ribociclib in combination with an aromatase inhibitor is not proven in patient group a1).

a2) Postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

Extent and probability of the additional benefit

Mortality

For the endpoint of overall survival, there was no statistically significant difference between the treatment groups at a median duration of observation of approx. 44 months, based on low event numbers.

Morbidity

*Recurrences (recurrence rate and invasive disease-free survival (iDFS)*

Patients in the present therapeutic indication are treated with a curative therapeutic approach. The failure of a curative therapeutic approach is fundamentally patient-relevant. The significance of the endpoints on recurrences depends on the extent to which the selected

individual components are suitable for adequately reflecting the failure of potential cure by the present curative therapeutic approach.

In the present benefit assessment, both the recurrence rate and the evaluation as iDFS are considered for recurrences. Both evaluations include the following events:

- death due to any cause,
- local breast cancer recurrence,
- regional invasive breast cancer recurrence,
- contralateral invasive breast cancer,
- distant recurrence and
- secondary primary cancer (not breast cancer)

This operationalisation is considered suitable for depicting a failure of the potential cure through the curative therapeutic approach.

Both the event rate and the time-to-event analysis showed a statistically significant difference between ribociclib in combination with an aromatase inhibitor and the control arm over a median duration of observation of approx. 44 months. Although the extent of the achieved advantage in recurrences is assessed as a relevant improvement, its extent is minimal.

*Symptomatology (EORTC QLQ-C30 and EORTC QLQ-BR23)*

In the NATALEE study, patient-reported symptomatology was collected using the EORTC QLQ-C30 and EORTC QLQ-BR23.

There were statistically significant differences between the treatment arms in the nausea and vomiting, pain and constipation scales of the QLQ-C30 and the side effects of systemic therapy scale of the QLQ-BR23. However, the 95% confidence interval of the standardised mean difference (SMD) is not completely outside the irrelevance range of -0.2 to 0.2 in any of the scales. Thus, it cannot be inferred that the observed effects are relevant. There were no statistically significant differences in the other scales and no suitable data on burden due to hair loss scale of the QLQ-BR23 are available due to the lack of a sufficiently high percentage of analysable female patients.

*Health status (EQ-5D VAS)*

Data on patient-reported health status was collected in the NATALEE study using the EQ-5D visual analogue scale.

The results do not show any statistically significant difference between the treatment groups.

In summary, in the endpoint category of morbidity, there is an advantage of ribociclib in combination with an aromatase inhibitor in the avoidance of recurrences. There were no statistically significant or relevant differences with regard to patient-reported symptomatology or health status.

Quality of life

*EORTC QLQ-C30 and EORTC QLQ-BR23*

There were no statistically significant differences between the treatment arms in the QLQ-C30 and QLQ-BR23 scales. No suitable data on the sexual pleasure scale of the QLQ-BR23 are available due to the lack of a sufficiently high percentage of analysable female patients.

Side effects

*Adverse events (AEs)*

In the NATALEE study, an adverse event occurred in 98% of female patients in the intervention arm and 87% thereof in the control arm. The results were only presented additionally.

*Serious adverse events (SAEs), severe adverse events (CTCAE grade ≥ 3) and discontinuation due to AEs*

For the endpoints of SAEs, severe AEs and discontinuation due to AEs, there was a statistically significant disadvantage of ribociclib in combination with an aromatase inhibitor compared to the control arm.

*Specific adverse events*

In detail, the specific AEs of neutropenia (PT, severe AE), gastrointestinal disorders (SOC, severe AE), skin and subcutaneous tissue disorders (SOC, AE), respiratory, thoracic and mediastinal disorders (SOC, AE), infections and infestations (SOC, severe AE), nervous system disorders (SOC, severe AE), fatigue (PT, severe AE), hepatobiliary toxicity (SMQ, severe AE) and nephrotoxicity (SMQ, severe AE) each showed a statistically significant difference to the disadvantage of ribociclib in combination with an aromatase inhibitor.

In summary, due to the disadvantages in the endpoints of SAEs, severe AEs and discontinuation due to AEs, a significant disadvantage in side effects can be identified overall for treatment with ribociclib in combination with an aromatase inhibitor.

Overall assessment

For the endpoint categories of mortality, morbidity, health-related quality of life and side effects, results from the open-label, randomised, controlled and currently ongoing NATALEE study are available for the benefit assessment of ribociclib in combination with an aromatase inhibitor for adjuvant treatment of premenopausal patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence.

For the endpoint of overall survival, there was no statistically significant difference between the treatment groups, based on low event numbers.

In the morbidity category, there was an advantage of ribociclib in combination with an aromatase inhibitor in the avoidance of recurrences. In the present curative treatment setting, the avoidance of recurrences is an essential therapeutic goal. There were no statistically significant or relevant differences with regard to patient-reported symptomatology or health status.

Likewise, there were no statistically significant differences in the health-related quality of life.

With regard to side effects, ribociclib in combination with an aromatase inhibitor showed statistically significant disadvantages for the endpoints of serious adverse events, severe adverse events, discontinuation due to AEs and in detail also for specific AEs.

In the overall analysis, the minor advantage in terms of recurrences was offset by significant disadvantages in terms of side effects. In a weighted decision, the G-BA came to the conclusion - against the background of the observed effect magnitude for recurrences - that the significant disadvantages in terms of side effects challenge the advantage in terms of recurrences. It is taken into account that the significance of the available results on recurrences is limited, especially since censoring occurred early and then continuously over the entire course and to a relevant extent. However, taking into account the clinical relevance, the disadvantage in terms of side effects also does not reach a level that would justify the derivation of a minor benefit in the overall assessment. It is therefore concluded that an

additional benefit of ribociclib in combination with an aromatase inhibitor is not proven in patient group a2).

a3) Men with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

The pharmaceutical company did not submit any data for the assessment of the additional benefit of ribociclib in combination with an aromatase inhibitor in patient group a3). An additional benefit is therefore proven.

### 2.1.4 Summary of the assessment

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

The therapeutic indication assessed here is as follows:

"Kisqali in combination with an aromatase inhibitor is indicated for the adjuvant treatment of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence.

In pre- or perimenopausal women, or in men, the aromatase inhibitor should be combined with a luteinising hormone-releasing hormone (LHRH) agonist."

The following three patient groups were differentiated in this therapeutic indication:

a1) Premenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

a2) Postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment as well as

a3) Men with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment.

On patient group a1)

The appropriate comparator therapy was determined to be tamoxifen (if applicable additionally with cessation of ovarian function) or abemaciclib in combination with endocrine therapy (only for female patients with node-positive breast cancer) or olaparib as monotherapy or in combination with endocrine therapy (only for female patients with germline BRCA1/2-mutations) or an aromatase inhibitor (anastrozole or letrozole or exemestane) in combination with cessation of ovarian function (exemestane only in combination with triptorelin).

For the evidence of additional benefit, the pharmaceutical company has submitted in the dossier the results on the sub-population of the still ongoing, open-label, randomised controlled trial NATALEE, which compared ribociclib in combination with anastrozole or letrozole with anastrozole or letrozole.

For the endpoint of overall survival, there was a relevant improvement but its extent was minimal.

In the morbidity category, there was an advantage of ribociclib in combination with an aromatase inhibitor in the avoidance of recurrences. There were no statistically significant or

relevant differences with regard to patient-reported symptomatology, health status as well as health-related quality of life.

With regard to side effects, there were statistically significant disadvantages for the endpoints of serious adverse events, severe adverse events, discontinuation due to AEs and in detail also for specific AEs.

In a weighted decision, the G-BA came to the conclusion - especially against the background of the observed effect magnitude for overall survival and recurrences - that the significant disadvantages in terms of side effects challenge the advantages in terms of overall survival and recurrences. It is thus found that an additional benefit is not proven for patient group a1).

On patient group a2)

The appropriate comparator therapy was determined to be an aromatase inhibitor (anastrozole or letrozole) alone, if applicable tamoxifen if aromatase inhibitors are unsuitable, or an aromatase inhibitor (anastrozole or exemestane) in sequence after tamoxifen or olaparib as monotherapy or in combination with endocrine therapy (only for female patients with germline BRCA1/2-mutations).

For the endpoint of overall survival, there was no statistically significant difference between the treatment groups, based on low event numbers.

In the morbidity category, there was an advantage of ribociclib in combination with an aromatase inhibitor in the avoidance of recurrences. There were no statistically significant or relevant differences with regard to patient-reported symptomatology, health status as well as health-related quality of life.

With regard to side effects, there were statistically significant disadvantages for the endpoints of serious adverse events, severe adverse events, discontinuation due to AEs and in detail also for specific AEs.

In a weighted decision, the G-BA came to the conclusion - especially against the background of the observed effect magnitude for recurrences - that the significant disadvantages in terms of side effects challenge the advantage in terms of recurrences. It is thus found that an additional benefit is not proven for patient group a2).

On patient group a3)

The appropriate comparator therapy was determined to be tamoxifen or abemaciclib in combination with endocrine therapy (only for male patients with node-positive breast cancer) or olaparib as monotherapy or in combination with endocrine therapy (only for male patients with germline BRCA1/2-mutations).

The pharmaceutical company did not submit any data for the assessment of the additional benefit of ribociclib in combination with an aromatase inhibitor in patient group a3). An additional benefit is therefore 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 resolution is based on the information from the dossier of the pharmaceutical company. The pharmaceutical company's approach is mathematically comprehensible but fraught with uncertainties. These result in particular from uncertainties regarding the triggering criteria

used and unclear transferability of percentage values to the patient groups in the individual derivation steps.

### 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 Kisqali (active ingredient: ribociclib) at the following publicly accessible link (last access: 22 April 2025):

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

Treatment with ribociclib should only be initiated and monitored by specialists in internal medicine, haematology, and oncology who are experienced in the treatment of patients with breast cancer, as well as specialists in obstetrics and gynaecology, and other specialists participating in the Oncology Agreement.

### 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 2025).

According to the product information for ribociclib, the aromatase inhibitor should be combined with an LHRH agonist in pre- or perimenopausal women and in men. Leuprorelin, triptorelin and goserelin are explicitly approved for use in women according to the respective product information. Against this background, LHRH agonists are not shown in the cost representation in patient group a3).

Treatment period:

According to the product information, ribociclib should be taken until completion of a 3-year treatment.

Abemaciclib should be taken without interruption for 2 years according to the product information.

According to the product information for olaparib, it is recommended that patients are treated with olaparib for up to one year.

For postmenopausal women with hormone receptor-positive early invasive breast cancer, the recommended duration of adjuvant endocrine therapy is 5 years in accordance with the product information for anastrozole.

In the adjuvant treatment of early hormone receptor-positive breast cancer, a treatment duration of at least 5 years is recommended for tamoxifen according to the product information.

In female patients with early breast cancer, treatment with exemestane should be continued in accordance with the product information until completion of the 5-year, combined, sequential, adjuvant hormone therapy.

In adjuvant therapy, treatment with letrozole should be continued for 5 years according to the product information.

a1) Premenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

| Designation of the therapy | Treatment mode | Number of treatments/ patient/ year | Treatment duration/ treatment (days) | Treatment days/ patient/ year |
|---|---|---|---|---|
| Medicinal product to be assessed | | | | |
| Ribociclib in combination with an aromatase inhibitor | | | | |
| Ribociclib | on day 1 - 21 of a 28-day cycle | 13.0 | 21 | 273.0 |
| Anastrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Letrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Exemestane | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Goserelin | 1 x every 28 days | 13.0 | 1 | 13.0 |
| Triptorelin | 1 x every 28 days | 13.0 | 1 | 13.0 |
| Leuprorelin | 1 x every 3 months | 4.0 | 1 | 4.0 |
| Appropriate comparator therapy | | | | |
| Tamoxifen (if necessary, in addition with cessation of ovarian function) | | | | |
| Tamoxifen | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| If applicable, LHRH agonist | | | | |
| Goserelin | 1 x every 28 days | 13.0 | 1 | 13.0 |
| Triptorelin | 1 x every 28 days | 13.0 | 1 | 13.0 |

| Designation of the therapy | Treatment mode | Number of treatments/ patient/ year | Treatment duration/ treatment (days) | Treatment days/ patient/ year |
|---|---|---|---|---|
| Leuprorelin | 1 x every 3 months | 4.0 | 1 | 4.0 |
| Abemaciclib in combination with endocrine therapy (only for female patients with node-positive breast cancer) | | | | |
| Abemaciclib | Continuously, 2 x daily | 365.0 | 1 | 365.0 |
| Anastrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Letrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Exemestane | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Tamoxifen | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Goserelin | 1 x every 28 days | 13.0 | 1 | 13.0 |
| Triptorelin | 1 x every 28 days | 13.0 | 1 | 13.0 |
| Leuprorelin | 1 x every 3 months | 4.0 | 1 | 4.0 |
| Olaparib as monotherapy or in combination with endocrine therapy (only for female patients with germline BRCA1/2-mutations) | | | | |
| Olaparib | Continuously, 2 x daily | 365 | 1 | 365 |
| Anastrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Letrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Exemestane | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Tamoxifen | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Goserelin | 1 x every 28 days | 13.0 | 1 | 13.0 |
| Triptorelin | 1 x every 28 days | 13.0 | 1 | 13.0 |

| Designation of the therapy | Treatment mode | Number of treatments/ patient/ year | Treatment duration/ treatment (days) | Treatment days/ patient/ year |
|---|---|---|---|---|
| Leuprorelin | 1 x every 3 months | 4.0 | 1 | 4.0 |
| An aromatase inhibitor (anastrozole or letrozole or exemestane) in combination with cessation of ovarian function (exemestane only in combination with triptorelin) | | | | |
| Anastrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Letrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Exemestane | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Goserelin | 1 x every 28 days | 13.0 | 1 | 13.0 |
| Triptorelin | 1 x every 28 days | 13.0 | 1 | 13.0 |
| Leuprorelin | 1 x every 3 months | 4.0 | 1 | 4.0 |

a2) Postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

| Designation of the therapy | Treatment mode | Number of treatments/ patient/ year | Treatment duration/ treatment (days) | Treatment days/ patient/ year |
|---|---|---|---|---|
| Medicinal product to be assessed | | | | |
| Ribociclib in combination with an aromatase inhibitor | | | | |
| Ribociclib | on day 1 - 21 of a 28-day cycle | 13.0 | 21 | 273.0 |
| Anastrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Letrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Exemestane | Continuously, 1 x daily | 365.0 | 1 | 365.0 |

| Designation of the therapy | Treatment mode | Number of treatments/ patient/ year | Treatment duration/ treatment (days) | Treatment days/ patient/ year |
|---|---|---|---|---|
| Appropriate comparator therapy | | | | |
| Aromatase inhibitor (anastrozole or letrozole) alone, or, if applicable, tamoxifen if aromatase inhibitors are unsuitable | | | | |
| Anastrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Letrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Tamoxifen | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Aromatase inhibitor (anastrozole or exemestane) in sequence after tamoxifen | | | | |
| Anastrozole in sequence after tamoxifen | | | | |
| Tamoxifen | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Anastrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Exemestane in sequence after tamoxifen | | | | |
| Tamoxifen | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Exemestane | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Olaparib as monotherapy or in combination with endocrine therapy (only for female patients with germline BRCA1/2-mutations) | | | | |
| Olaparib | Continuously, 2 x daily | 365 | 1 | 365 |
| Anastrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Letrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Exemestane | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Tamoxifen | Continuously, 1 x daily | 365.0 | 1 | 365.0 |

a3) Men with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

| Designation of the therapy | Treatment mode | Number of treatments/ patient/ year | Treatment duration/ treatment (days) | Treatment days/ patient/ year |
|---|---|---|---|---|
| Medicinal product to be assessed | | | | |
| Ribociclib in combination with an aromatase inhibitor | | | | |
| Ribociclib | on day 1 - 21 of a 28-day cycle | 13.0 | 21 | 273.0 |
| Anastrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Letrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Exemestane | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Appropriate comparator therapy | | | | |
| Tamoxifen | | | | |
| Tamoxifen | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Abemaciclib in combination with endocrine therapy (only for patients with node-positive breast cancer) | | | | |
| Abemaciclib | Continuously, 2 x daily | 365.0 | 1 | 365.0 |
| Anastrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Letrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Exemestane | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Tamoxifen | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Olaparib as monotherapy or in combination with endocrine therapy (only for male patients with germline BRCA1/2-mutations) | | | | |
| Olaparib | Continuously, 2 x daily | 365 | 1 | 365 |

| Designation of the therapy | Treatment mode | Number of treatments/ patient/ year | Treatment duration/ treatment (days) | Treatment days/ patient/ year |
|---|---|---|---|---|
| Anastrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Letrozole | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Exemestane | Continuously, 1 x daily | 365.0 | 1 | 365.0 |
| Tamoxifen | Continuously, 1 x daily | 365.0 | 1 | 365.0 |

Consumption:

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

a1) Premenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

| 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 | | | | | |
| Ribociclib in combination with an aromatase inhibitor | | | | | |
| Ribociclib | 400 mg | 400 mg | 2 x 200 mg | 273.0 | 546 x 200 mg |
| Anastrozole | 1 mg | 1 mg | 1 x 1 mg | 365.0 | 365 x 1 mg |
| Letrozole | 2.5 mg | 2.5 mg | 1 x 2.5 mg | 365.0 | 365 x 2.5 mg |
| Exemestane | 25 mg | 25 mg | 1 x 25 mg | 365.0 | 365 x 25 mg |
| Goserelin | 3.6 mg | 3.6 mg | 1 x 3.6 mg | 13.0 | 13 x 3.6 mg |
| Triptorelin | 3.75 mg | 3.75 mg | 1 x 3.75 mg | 13.0 | 13 x 3.75 mg |
| Leuprorelin | 11.25 mg | 11.25 mg | 1 x 11.25 mg | 4.0 | 4 x 11.25 mg |
| Appropriate comparator therapy | | | | | |
| Tamoxifen (if necessary, in addition with cessation of ovarian function) | | | | | |
| Tamoxifen | 20 mg | 20 mg | 1 x 20 mg | 365.0 | 365 x 20 mg |

| Designation of the therapy | Dosage/ application | Dose/ patient/ treatment days | Consumption by potency/ treatment day | Treatment days/ patient/ year | Average annual consumption by potency |
|---|---|---|---|---|---|
| If applicable, LHRH agonist | | | | | |
| Goserelin | 3.6 mg | 3.6 mg | 1 x 3.6 mg | 13.0 | 13 x 3.6 mg |
| Triptorelin | 3.75 mg | 3.75 mg | 1 x 3.75 mg | 13.0 | 13 x 3.75 mg |
| Leuprorelin | 11.25 mg | 11.25 mg | 1 x 11.25 mg | 4.0 | 4 x 11.25 mg |
| Abemaciclib in combination with endocrine therapy (only for female patients with node-positive breast cancer) | | | | | |
| Abemaciclib | 150 mg | 300 mg | 2 x 150 mg | 365.0 | 730 x 150 mg |
| Anastrozole | 1 mg | 1 mg | 1 x 1 mg | 365.0 | 365 x 1 mg |
| Letrozole | 2.5 mg | 2.5 mg | 1 x 2.5 mg | 365.0 | 365 x 2.5 mg |
| Exemestane | 25 mg | 25 mg | 1 x 25 mg | 365.0 | 365 x 25 mg |
| Tamoxifen | 20 mg | 20 mg | 1 x 20 mg | 365.0 | 365 x 20 mg |
| Goserelin | 3.6 mg | 3.6 mg | 1 x 3.6 mg | 13.0 | 13 x 3.6 mg |
| Triptorelin | 3.75 mg | 3.75 mg | 1 x 3.75 mg | 13.0 | 13 x 3.75 mg |
| Leuprorelin | 11.25 mg | 11.25 mg | 1 x 11.25 mg | 4.0 | 4 x 11.25 mg |
| Olaparib as monotherapy or in combination with endocrine therapy (only for female patients with germline BRCA1/2-mutations) | | | | | |
| Olaparib | 300 mg | 600 mg | 6 x 100 mg | 365.0 | 2,190 x 100 mg |
| Anastrozole | 1 mg | 1 mg | 1 x 1 mg | 365.0 | 365 x 1 mg |
| Letrozole | 2.5 mg | 2.5 mg | 1 x 2.5 mg | 365.0 | 365 x 2.5 mg |
| Exemestane | 25 mg | 25 mg | 1 x 25 mg | 365.0 | 365 x 25 mg |
| Tamoxifen | 20 mg | 20 mg | 1 x 20 mg | 365.0 | 365 x 20 mg |
| Goserelin | 3.6 mg | 3.6 mg | 1 x 3.6 mg | 13.0 | 13 x 3.6 mg |
| Triptorelin | 3.75 mg | 3.75 mg | 1 x 3.75 mg | 13.0 | 13 x 3.75 mg |
| Leuprorelin | 11.25 mg | 11.25 mg | 1 x 11.25 mg | 4.0 | 4 x 11.25 mg |
| An aromatase inhibitor (anastrozole or letrozole or exemestane) in combination with cessation of ovarian function (exemestane only in combination with triptorelin) | | | | | |
| Anastrozole | 1 mg | 1 mg | 1 x 1 mg | 365.0 | 365 x 1 mg |
| Letrozole | 2.5 mg | 2.5 mg | 1 x 2.5 mg | 365.0 | 365 x 2.5 mg |
| Exemestane | 25 mg | 25 mg | 1 x 25 mg | 365.0 | 365 x 25 mg |

| Designation of the therapy | Dosage/ application | Dose/ patient/ treatment days | Consumption by potency/ treatment day | Treatment days/ patient/ year | Average annual consumption by potency |
|---|---|---|---|---|---|
| Goserelin | 3.6 mg | 3.6 mg | 1 x 3.6 mg | 13.0 | 13 x 3.6 mg |
| Triptorelin | 3.75 mg | 3.75 mg | 1 x 3.75 mg | 13.0 | 13 x 3.75 mg |
| Leuprorelin | 11.25 mg | 11.25 mg | 1 x 11.25 mg | 4.0 | 4 x 11.25 mg |

a2) Postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

| 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 | | | | | |
| Ribociclib in combination with an aromatase inhibitor | | | | | |
| Ribociclib | 400 mg | 400 mg | 2 x 200 mg | 273.0 | 546 x 200 mg |
| Anastrozole | 1 mg | 1 mg | 1 x 1 mg | 365.0 | 365 x 1 mg |
| Letrozole | 2.5 mg | 2.5 mg | 1 x 2.5 mg | 365.0 | 365 x 2.5 mg |
| Exemestane | 25 mg | 25 mg | 1 x 25 mg | 365.0 | 365 x 25 mg |
| Appropriate comparator therapy | | | | | |
| Aromatase inhibitor (anastrozole or letrozole) alone, or, if applicable, tamoxifen if aromatase inhibitors are unsuitable | | | | | |
| Tamoxifen | 20 mg | 20 mg | 1 x 20 mg | 365.0 | 365 x 20 mg |
| Anastrozole | 1 mg | 1 mg | 1 x 1 mg | 365.0 | 365 x 1 mg |
| Letrozole | 2.5 mg | 2.5 mg | 1 x 2.5 mg | 365.0 | 365 x 2.5 mg |
| Aromatase inhibitor (anastrozole or exemestane) in sequence after tamoxifen | | | | | |
| Anastrozole in sequence after tamoxifen | | | | | |
| Tamoxifen | 20 mg | 20 mg | 1 x 20 mg | 365.0 | 365 x 20 mg |
| Anastrozole | 1 mg | 1 mg | 1 x 1 mg | 365.0 | 365 x 1 mg |
| Exemestane in sequence after tamoxifen | | | | | |
| Tamoxifen | 20 mg | 20 mg | 1 x 20 mg | 365.0 | 365 x 20 mg |
| Exemestane | 25 mg | 25 mg | 1 x 25 mg | 365.0 | 365 x 25 mg |

| Designation of the therapy | Dosage/ application | Dose/ patient/ treatment days | Consumption by potency/ treatment day | Treatment days/ patient/ year | Average annual consumption by potency |
|---|---|---|---|---|---|
| Olaparib as monotherapy or in combination with endocrine therapy (only for female patients with germline BRCA1/2-mutations) | | | | | |
| Olaparib | 300 mg | 600 mg | 6 x 100 mg | 365.0 | 2,190 x 100 mg |
| Anastrozole | 1 mg | 1 mg | 1 x 1 mg | 365.0 | 365 x 1 mg |
| Letrozole | 2.5 mg | 2.5 mg | 1 x 2.5 mg | 365.0 | 365 x 2.5 mg |
| Exemestane | 25 mg | 25 mg | 1 x 25 mg | 365.0 | 365 x 25 mg |
| Tamoxifen | 20 mg | 20 mg | 1 x 20 mg | 365.0 | 365 x 20 mg |

a3) Men with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

| Designation of the therapy | Dosage/ application | Dosage/ patient/ treatment days | Consumption by potency/ treatment day | Treatment days/ patient/ year | Average annual consumption by potency |
|---|---|---|---|---|---|
| Medicinal product to be assessed | | | | | |
| Ribociclib in combination with an aromatase inhibitor | | | | | |
| Ribociclib | 400 mg | 400 mg | 2 x 200 mg | 273.0 | 546 x 200 mg |
| Anastrozole | 1 mg | 1 mg | 1 x 1 mg | 365.0 | 365 x 1 mg |
| Letrozole | 2.5 mg | 2.5 mg | 1 x 2.5 mg | 365.0 | 365 x 2.5 mg |
| Exemestane | 25 mg | 25 mg | 1 x 25 mg | 365.0 | 365 x 25 mg |
| Appropriate comparator therapy | | | | | |
| Tamoxifen | | | | | |
| Tamoxifen | 20 mg | 20 mg | 1 x 20 mg | 365.0 | 365 x 20 mg |
| Abemaciclib in combination with endocrine therapy (only for patients with node-positive breast cancer) | | | | | |
| Abemaciclib | 150 mg | 300 mg | 2 x 150 mg | 365.0 | 730 x 150 mg |
| Anastrozole | 1 mg | 1 mg | 1 x 1 mg | 365.0 | 365 x 1 mg |
| Letrozole | 2.5 mg | 2.5 mg | 1 x 2.5 mg | 365.0 | 365 x 2.5 mg |
| Exemestane | 25 mg | 25 mg | 1 x 25 mg | 365.0 | 365 x 25 mg |

| Designation of the therapy | Dosage/ application | Dosage/ patient/ treatment days | Consumption by potency/ treatment day | Treatment days/ patient/ year | Average annual consumption by potency |
|---|---|---|---|---|---|
| Tamoxifen | 20 mg | 20 mg | 1 x 20 mg | 365.0 | 365 x 20 mg |
| Olaparib as monotherapy or in combination with endocrine therapy (only for female patients with germline BRCA1/2-mutations) | | | | | |
| Olaparib | 300 mg | 600 mg | 6 x 100 mg | 365.0 | 2,190 x 100 mg |
| Anastrozole | 1 mg | 1 mg | 1 x 1 mg | 365.0 | 365 x 1 mg |
| Letrozole | 2.5 mg | 2.5 mg | 1 x 2.5 mg | 365.0 | 365 x 2.5 mg |
| Exemestane | 25 mg | 25 mg | 1 x 25 mg | 365.0 | 365 x 25 mg |
| Tamoxifen | 20 mg | 20 mg | 1 x 20 mg | 365.0 | 365 x 20 mg |

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Sections 130 and 130 a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. Any reference prices 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 | | | | | |
| Ribociclib 400 mg | 42 FCT | € 2,320.48 | € 1.77 | € 0.00 | € 2,318.71 |
| Anastrozole 1 mg[3] | 100 FCT | € 43.68 | € 1.77 | € 2.56 | € 39.35 |
| Letrozole 2.5 mg[3] | 100 FCT | € 53.48 | € 1.77 | € 3.33 | € 48.38 |
| Exemestane 25 mg[3] | 100 FCT | € 127.53 | € 1.77 | € 9.19 | € 116.57 |
| Goserelin 3.6 mg | 3 IMP | € 632.16 | € 1.77 | € 34.37 | € 596.02 |
| Triptorelin 3.75 mg | 1 DSS | € 231.94 | € 1.77 | € 27.92 | € 202.25 |
| Leuprorelin 11.25 mg | 2 SRM | € 1010.55 | € 1.77 | € 55.32 | € 953.46 |
| Appropriate comparator therapy | | | | | |
| Anastrozole 1 mg[3] | 100 FCT | € 43.68 | € 1.77 | € 2.56 | € 39.35 |

[3] Fixed reimbursement rate

| 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 |
|---|---|---|---|---|---|
| Letrozole 2.5 mg[3] | 100 FCT | € 53.48 | € 1.77 | € 3.33 | € 48.38 |
| Exemestane 25 mg[3] | 100 FCT | € 127.53 | € 1.77 | € 9.19 | € 116.57 |
| Goserelin 3.6 mg | 3 IMP | € 632.16 | € 1.77 | € 34.37 | € 596.02 |
| Triptorelin 3.75 mg | 1 DSS | € 231.94 | € 1.77 | € 27.92 | € 202.25 |
| Leuprorelin 11.25 mg | 2 SRM | € 1010.55 | € 1.77 | € 55.32 | € 953.46 |
| Tamoxifen 20 mg[3] | 100 TAB | € 28.05 | € 1.77 | € 1.32 | € 24.96 |
| Abemaciclib 150 mg | 168 FCT | € 6,338.77 | € 1.77 | € 358.72 | € 5,978.28 |
| Olaparib 300 mg | 112 FCT | € 3,194.79 | € 1.77 | € 179.16 | € 3,013.86 |
| Abbreviations: FCT = film-coated tablets; IMP = implant; SRM = sustained-release microcapsules and suspending agents; TAB = tablets; DSS = dry substance with solvent | | | | | |

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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.

## 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 requirements 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:

a1) Premenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

No medicinal product with new active ingredients that can be used in a combination therapy and fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.
References:
Product information for ribociclib (Kisqali); Kisqali® 200 mg film-coated tablets; last revised: November 2024

a2) Postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

No medicinal product with new active ingredients that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.
References:
Product information for ribociclib (Kisqali); Kisqali® 200 mg film-coated tablets; last revised: November 2024

a3) Men with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative early breast cancer at high risk of recurrence; adjuvant treatment

No medicinal product with new active ingredients that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.
References:
Product information for ribociclib (Kisqali); Kisqali® 200 mg film-coated tablets; last revised: November 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 their session on 12 June 2019, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place once the positive opinion was granted. The Subcommittee on Medicinal Products determined the appropriate comparator therapy at their session on 26 November 2024.

On 16 December 2024, the pharmaceutical company submitted a dossier for the benefit assessment of ribociclib to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO number 2.

By letter dated 17 December 2024 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 ribociclib.

The dossier assessment by the IQWiG was submitted to the G-BA on 13 March 2025, and the written statement procedure was initiated with publication on the G-BA website on 17 March 2025. The deadline for submitting statements was 17 April 2025.

The oral hearing was held on 22 April 2025.

By letter dated 23 April 2025, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by IQWiG was submitted to the G-BA on 12 May 2025.

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 27 May 2025, and the proposed draft resolution was approved.

At their session on 5 June 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

**Chronological course of consultation**

| Session | Date | Subject of consultation |
|---|---|---|
| Subcommittee on Medicinal Products | 12 June 2019 | Determination of the appropriate comparator therapy |
| Subcommittee on Medicinal Products | 26 November 2024 | New determination of the appropriate comparator therapy |
| Working group Section 35a | 15 April 2025 | Information on written statements received; preparation of the oral hearing |
| Subcommittee on Medicinal Products | 22 April 2025 | Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents |
| Working group Section 35a | 29 April 2025<br>13 May 2025 | Consultation on the dossier evaluation by the IQWiG and evaluation of the written statement procedure |
| Subcommittee on Medicinal Products | 27 May 2025 | Concluding discussion of the draft resolution |
| Plenum | 5 June 2025 | Adoption of the resolution on the amendment of the Pharmaceuticals Directive |

Berlin, 5 June 2025

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

Prof. Hecken