Gemeinsamer Bundesausschuss

Justification

for 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

Abemaciclib (reassessment after the deadline: breast cancer, HR+, HER2-, early at high risk of recurrence, adjuvant treatment, combination with endocrine therapy)

From 20 August 2026

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assess 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 studies the pharmaceutical company have 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 decide 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 pharmaceutical company submitted a dossier for the early benefit assessment of the active ingredient abemaciclib (Verzenios) on 26 April 2022. The resolution adopted in this procedure by the G-BA on 20 October 2022 for patient populations a1) (premenopausal women within the therapeutic indication) and a2) (postmenopausal women within the therapeutic indication) was limited until 1 July 2025. At the request of the pharmaceutical company, this time limit was extended until 1 July 2026 by resolution of the G-BA dated 6 March 2025.

In accordance with Section 4, paragraph 3, number 5 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 5 of the Rules of Procedure (VerfO), the benefit assessment procedure for the medicinal product Verzenios recommences upon expiry of the deadline.

Pursuant to Section 4, paragraph 3, number 5 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 5 of the Rules of Procedure (VerfO), the pharmaceutical company submitted the final dossier to the G-BA on 27 February 2026.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 June 2026 on the G-BA website at (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 abemaciclib 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, the statements submitted in the written statement and oral hearing procedure, and the addendum to the benefit assessment prepared by IQWiG. In order to determine the extent of the additional benefit, the G-BA have 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 abemaciclib.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA have made 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 abemaciclib (Verzenios) in accordance with the product information

Verzenios in combination with endocrine therapy is indicated for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive early breast cancer at high risk of recurrence.

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

Therapeutic indication of the resolution (resolution of 20.08.2026):

Verzenios in combination with endocrine therapy is indicated for the adjuvant treatment of premenopausal and postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive early breast cancer at high risk of recurrence.

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

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

a1) Premenopausal women with HR-positive, HER2-negative, node-positive early breast cancer at high risk of recurrence; adjuvant treatment

Appropriate comparator therapy for abemaciclib in combination with an endocrine therapy:

[1] General Methods, version 8.0 from 19.12.2025. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

- tamoxifen (if applicable, with additional ovarian function suppression)

or

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

or

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

or

- ribociclib in combination with an aromatase inhibitor

a2) Postmenopausal women with HR-positive, HER2-negative, node-positive early breast cancer at high risk of recurrence; adjuvant treatment

Appropriate comparator therapy for abemaciclib in combination with an endocrine therapy:

- 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 female patients with germline BRCA1/2-mutations are eligible)

or

- ribociclib in combination with an aromatase inhibitor

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 according to 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 they determine 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 for 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 for 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.

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

On 1. In addition to abemaciclib, medicinal products with the active ingredients tamoxifen, anastrozole, exemestane, letrozole, leuprorelin, goserelin, triptorelin, cyclophosphamide, docetaxel, doxorubicin, epirubicin, fluorouracil, methotrexate, paclitaxel, vincristine, ribociclib and olaparib are approved for 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 are considered as non-medicinal treatments in the present therapeutic indication.

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

On 3. The resolution of 20 October 2022 on the benefit assessment of medicinal products with new active ingredients pursuant to Section 35a SGB V for abemaciclib in the therapeutic indication of HR-positive, HER2-negative early breast cancer at high risk of recurrence is replaced by the present resolution for patient populations a1 and a2.

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

- Olaparib (as monotherapy or in combination with endocrine therapy): Resolution of 16 February 2023
- Ribociclib (in combination with aromatase inhibitor): Resolution of 5 June 2025

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

Guideline on Examination and Treatment Methods in Hospitals (Hospital Treatment Methods Policy) – Methods excluded from provision at the expense of the statutory health insurance:

- 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 DMPs for female patients with breast cancer

Guideline on SHI-accredited healthcare methods: Biomarker-based tests for deciding for or against adjuvant systemic chemotherapy for primary breast cancer

Pharmaceuticals Directive, Annex VI (off-label use)

- Part A: XXXVII. Bisphosphonates in patients with hormone receptor (HR)-positive, postmenopausal breast cancer: adjuvant bisphosphonate therapy in patients with hormone receptor (HR)-positive, postmenopausal breast cancer
- Part B: IV. Gemcitabine as 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.

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 - where indicated - has been completed. There are different recommendations for adjuvant endocrine therapy for premenopausal and postmenopausal women.

Premenopausal women

In the adjuvant treatment of hormone receptor (HR)-positive breast cancer in premenopausal women, guidelines recommend tamoxifen, with additional ovarian function suppression to be considered. Given that the present therapeutic indication explicitly covers female patients at high risk of recurrence, it is established that the appropriate comparator therapy may include ovarian function suppression in addition to tamoxifen.

In addition, the guidelines recommend the active ingredient ribociclib. Ribociclib is approved for the adjuvant treatment of HR-positive, HER-2 negative early breast cancer at high risk of recurrence. In the benefit assessment, it was established by the resolution of 5 June 2025 that an additional benefit for premenopausal women is not proven. In accordance with the marketing authorisation, ribociclib in combination with endocrine therapy is considered an equally appropriate comparator therapy for premenopausal patients.

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 established by the resolution of 16 February 2023. In accordance with the marketing authorisation, the appropriate comparator therapy also includes olaparib.

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). According to statements by clinical experts in an earlier benefit assessment procedure in a similar therapeutic indication, aromatase inhibitors in combination with ovarian function suppression 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 ovarian function suppression are also determined as an appropriate comparator therapy, with exemestane having only been approved in combination with triptorelin.

Postmenopausal women

Aromatase inhibitors assume a high significance in the adjuvant treatment of HR-positive breast cancer in postmenopausal women. The two non-steroidal aromatase inhibitors anastrozole and letrozole have been granted marketing authorisation 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 an appropriate comparator therapy for initial adjuvant treatment.

In case of intolerance to an aromatase inhibitor, tamoxifen is the recommended alternative for (further) adjuvant treatment. In addition to aromatase inhibitor (anastrozole or letrozole) monotherapy or 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 shows 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.

In addition, the guidelines recommend the active ingredient ribociclib. In the benefit assessment, it was established by the resolution of 5 June 2025 that an additional benefit is not proven for postmenopausal women. In accordance with the marketing authorisation, ribociclib in combination with endocrine therapy is considered an equally appropriate comparator therapy for postmenopausal patients.

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 the resolution of 16 February 2023, an indication of a minor additional benefit was established. In accordance with the marketing authorisation, the appropriate comparator therapy also includes olaparib.

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 with hormone receptor-positive breast cancer.

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

Any change to the appropriate comparator therapy requires a decision by the G-BA based on a prior review of the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO.

2.1.3 Extent and probability of the additional benefit

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

a1) Premenopausal women with HR-positive, HER2-negative, node-positive early breast cancer at high risk of recurrence; adjuvant treatment

Hint of a minor additional benefit

a2) Postmenopausal women with HR-positive, HER2-negative, node-positive early breast cancer at high risk of recurrence; adjuvant treatment

An additional benefit is not proven.

Justification:

To demonstrate an additional benefit, the pharmaceutical company submitted the dossier with the results of the still ongoing, open-label, randomised controlled trial MONARCH-E, which compared abemaciclib in combination with standard endocrine therapy versus standard endocrine therapy.

[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

The MONARCH-E study has been ongoing since July 2017 at 611 study sites in Asia, Australia, Europe, North America and South America.

Patients with node-positive, HR-positive, HER2-negative, definitely resected early breast cancer at high risk of recurrence without distant metastases were enrolled in the study.

The MONARCH-E study is divided into 2 cohorts. In cohort 1, high risk of recurrence is defined as ≥ 4 positive axillary lymph nodes (pALN) or 1 to 3 pALN in the presence of an additional grade 3 tumour and/or a tumour size ≥ 5 cm (corresponding to stage IIA to IIIC at diagnosis). The definition of a high risk of recurrence for cohort 1 is considered adequate for the benefit assessment. In cohort 2, a high risk of recurrence was determined primarily on the basis of the proliferation marker Ki-67. Cohort 2 is not considered relevant for the benefit assessment as the marketing authorisation was granted solely on the basis of the results for cohort 1.

A total of 5,120 patients were enrolled in cohort 1 and randomised in a 1:1 ratio to the intervention arm (N = 2,555) and the comparator arm (N = 2,565), stratified by previous treatment (neoadjuvant chemotherapy vs adjuvant chemotherapy vs no chemotherapy), menopausal status (premenopausal vs postmenopausal), region (North America and Europe vs Asia vs others).

In both study arms, the patients received standard adjuvant endocrine therapy according to the doctor's instructions, which was to be continued for at least 5 years where medically indicated. Patients in the intervention arm also received abemaciclib for 2 years following randomisation. Patients enrolled in the study may have already started adjuvant endocrine therapy before the start of the study. However, they should be randomised within 12 weeks of the start of endocrine therapy. The remaining patients began their endocrine therapy at the start of the study.

As part of the written statement procedure, the pharmaceutical company submitted analyses of the sub-populations of all pre- and postmenopausal patients who, at the start of the study, were being treated with endocrine therapy in accordance with the appropriate comparator therapy. This population (i.e. corresponding to the ITT population) is used for the present assessment.

The primary endpoint of the study is invasive disease-free survival (IDFS, hereafter also referred to as recurrences). Endpoints in the categories of mortality, morbidity, health-related quality of life and side effects were also assessed.

The results of the 7th data cut-off (final data cut-off for overall survival) from 15.07.2025 for the endpoints of overall survival, failure of the curative therapeutic approach and side effects are used for the present assessment. For the other endpoints of morbidity and health-related quality of life, the 5th data cut-off from 01.07.2022 was considered.

<u>On the implementation of time limit requirements</u>

According to the justification for the resolution of 20 October 2022, the limitation was based on the fact that further relevant clinical data for the benefit assessment, in particular on overall survival and recurrences, were expected from the MONARCH-E study.

For the new benefit assessment after expiry of the deadline, the results on all patient-relevant endpoints for the patient populations a1 and a2 of the MONARCH-E study must be submitted in the dossier at the final data cut-off.

With the pharmaceutical company having presented the required analyses in the dossier, the time limit requirements are considered to have been met overall.

<u>Extent and probability of the additional benefit</u>

a1) Premenopausal women with HR-positive, HER2-negative, node-positive early breast cancer at high risk of recurrence; adjuvant treatment

Mortality

Overall survival was defined in the MONARCH-E study as the time between randomisation and death from any cause.

For the endpoint of overall survival, there was a statistically significant difference to the advantage of abemaciclib in combination with endocrine therapy compared to the control arm.

The extent of the achieved extension in overall survival is rated as a relevant, yet minor, improvement.

Morbidity

Recurrences (recurrence rate and disease-free survival (DFS))

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 analysis as DFS are considered for recurrences. Both analyses include the following events:

- Local breast cancer recurrence
- Regional invasive breast cancer recurrence
- Distant recurrence
- Contralateral invasive breast cancer
- Secondary primary cancer (not breast cancer)
- Death from any cause

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

For the "recurrence rate" and "disease-free survival" endpoint components of the "recurrences" endpoint, there was a statistically significant difference in each case to the advantage of abemaciclib in combination with endocrine therapy compared to endocrine therapy.

Overall, analysis of both endpoint components showed only a relevant, yet minor, advantage of abemaciclib in combination with endocrine therapy in terms of preventing recurrences.

Symptomatology (FACIT-Fatigue)

In the MONARCH-E study, the endpoint of symptomatology was assessed using the validated survey instrument FACIT-Fatigue.

In the dossier, the pharmaceutical company submitted analyses of the course and change of symptomatology from baseline using a mixed model for repeated measures (MMRM). However, there are discrepancies in the data on the number of female patients included in the respective analyses at individual survey time points. Furthermore, no data are available on the total number of patients included in the MMRM analyses. Given the patient numbers indicated for each measurement time point in the tabulated changes from baseline, the

MMRM analyses were assumed to include a sufficient number of patients and were therefore used despite the limitations mentioned.

Consequently, for the endpoint of symptomatology, there was a statistically significant difference to the disadvantage of abemaciclib in combination with endocrine therapy. However, it cannot be inferred that the observed effect is relevant as the 95% CI of the standardised mean difference does not lie entirely outside the irrelevance range of –0.2 to 0.2.

Health status (EQ-5D visual analogue scale)

The health status was assessed using the visual analogue scale (VAS) of the EQ-5D questionnaire.

For the endpoint of health status, the pharmaceutical company provided the dossier with MMRM analyses of the course and change of symptomatology from baseline. For the symptomatology endpoint (FACIT-Fatigue) as already explained above, these MMRM analyses are used for the benefit assessment.

As a result, for the endpoint of health status, assessed using the EQ-5D VAS, there was no statistically significant difference between the treatment groups.

In summary, in the endpoint category of morbidity, there was a relevant, yet minor, advantage in terms of preventing recurrences. With regard to symptomatology (FACIT-Fatigue) , there was a statistically significant difference to the disadvantage of abemaciclib in combination with endocrine therapy. However, it cannot be inferred that the observed effect is relevant. There is neither an advantage nor a disadvantage for the endpoint of health status. In the endpoint category of morbidity, an advantage of abemaciclib in combination with endocrine therapy was observed overall.

Quality of life

Functional Assessment of Cancer Therapy – Endocrine Symptoms (FACT-ES)

The FACT-ES comprises the FACT-G scales and the endocrine symptom scale ESS-19, for which a total score is to be calculated. However, the pharmaceutical company only submitted the results of the subscale ESS-19 for the analysis of the FACT-ES. The additionally presented ESS-18 subscale corresponds to the ESS-19 scale with the final question omitted. This analysis also fails to comply with the guidelines for evaluating the FACT-ES.

The ESS-19 and ESS-18 are not used for the benefit assessment.

Functional Assessment of Cancer Therapy – Breast (FACT-B)

Health-related quality of life is also assessed in the study using the disease-specific FACT-B questionnaire. The FACT-B questionnaire consists of the cross-tumour disease questionnaire (FACT-G) and a breast cancer-specific subscale (BCS). Only the FACT-B total score is included in the assessment of the additional benefit as it considers the data on the health-related quality of life of the patients.

The pharmaceutical company provided the FACT-B dossier with MMRM analyses of the course and change in the health-related quality of life from baseline. For the symptomatology endpoint (FACIT-Fatigue) as already explained above, these MMRM analyses are used for the benefit assessment.

Consequently, for the endpoint of health-related quality of life, there was a statistically significant difference to the disadvantage of abemaciclib in combination with endocrine therapy. However, it cannot be inferred that the observed effect is relevant as the 95% CI of

the standardised mean difference does not lie entirely outside the irrelevance range of –0.2 to 0.2.

In summary, in the quality of life category, there was a statistically significant difference to the disadvantage of abemaciclib in combination with endocrine therapy. However, it cannot be inferred that the observed effect is relevant. Overall, neither an advantage nor a disadvantage of abemaciclib in combination with endocrine therapy in terms of the quality of life was observed.

Side effects

Adverse events (AEs)

In the MONARCH-E study, an adverse event occurred in 98% of the female patients in the intervention arm and 89% of those 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 abemaciclib in combination with endocrine therapy compared to the control arm in each case.

Specific adverse events

For the specific AEs of neutropenia (severe AEs), eye disorders (AEs), skin and subcutaneous tissue disorders (AEs), gastrointestinal disorders (severe AEs), diarrhoea (severe AEs), general disorders and administration site conditions (severe AEs), hepatobiliary disorders (severe AEs), physical examinations (severe AEs), metabolism and nutrition disorders (severe AEs) and respiratory, thoracic and mediastinal disorders (severe AEs), there was a statistically significant difference in each case to the disadvantage of abemaciclib in combination with endocrine therapy.

For the endpoint of genital and mammary gland disorders (severe AEs), there was a significant difference to the advantage of abemaciclib in combination with endocrine therapy.

In summary, the disadvantages for the endpoints of SAEs, severe AEs and discontinuation due to AEs lead to an overall significant disadvantage of the treatment with abemaciclib in combination with endocrine therapy in terms of side effects. Detailed analysis also showed disadvantages in terms of the specific adverse events.

Overall assessment

Results on the endpoint categories of mortality, morbidity, health-related quality of life and side effects from the ongoing, open-label, randomised controlled trial MONARCH-E are available for the benefit assessment of abemaciclib in combination with endocrine therapy for the treatment of HR-positive, HER2-negative early breast cancer at high risk of recurrence in premenopausal patients.

For the endpoint of overall survival, there was a statistically significant advantage of abemaciclib in combination with endocrine therapy, which is rated overall as a relevant, yet minor, improvement.

In the endpoint category of morbidity, there was a relevant, yet minor, advantage of abemaciclib in combination with endocrine therapy in terms of preventing recurrences. In the present curative treatment setting, the prevention of recurrences is a very relevant

therapeutic goal. For symptomatology (FACIT-Fatigue), there was a statistically significant difference to the disadvantage of abemaciclib in combination with endocrine therapy. However, it cannot be inferred that the observed effect is relevant. For the endpoint of health status (EQ-5D VAS), there was neither an advantage nor a disadvantage. An advantage of abemaciclib in combination with endocrine therapy was derived overall.

For the health-related quality of life (FACT-B), there was a statistically significant difference to the disadvantage of abemaciclib in combination with endocrine therapy. However, it cannot be inferred that the observed effect is relevant. For the health-related quality of life, neither an advantage nor a disadvantage could therefore be observed.

With regard to side effects, an overall significant disadvantage of abemaciclib in combination with endocrine therapy can be observed due to the disadvantages for the endpoints of serious adverse events, severe adverse events and discontinuation due to AEs, as well as the specific AEs.

In the overall analysis of the available results, the relevant, yet minor, improvement in overall survival and the relevant, yet minor, advantage in terms of preventing recurrences are offset by significant disadvantages in terms of side effects. In a weighted decision as part of the overall assessment, the G-BA concluded that there was a moderate – and not merely minor – improvement in treatment-related benefit and, consequently, a minor additional benefit of abemaciclib in combination with endocrine therapy compared with endocrine therapy alone.

Reliability of data (probability of the additional benefit)

The open-label, randomised controlled trial MONARCH-E forms the basis of this benefit assessment.

With regard to the endpoints of overall survival and failure of the curative therapeutic approach, the risk of bias is rated as high, since censoring events occurred to a significant extent early on and then continuously throughout the study. Administrative censoring events, e.g., due to data cut-offs, are relatively less relevant during this period. The reasons for early censoring remain largely unclear.

The endpoint-specific risk of bias for the results of the patient-reported endpoints on morbidity and health-related quality of life is rated as high due to the open-label study design.

Thus, the reliability of data for the additional benefit determined is classified in the "hint" category overall.

a2) Postmenopausal women with HR-positive, HER2-negative, node-positive early breast cancer at high risk of recurrence; adjuvant treatment

Mortality

Overall survival was defined in the MONARCH-E study as the time between randomisation and death from any cause.

For the endpoint of overall survival, there was no statistically significant difference between the two treatment groups.

Morbidity

Recurrences (recurrence rate and disease-free survival)

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 analysis as DFS are considered for recurrences. Both analyses include the following events:

- Local breast cancer recurrence
- Regional invasive breast cancer recurrence
- Distant recurrence
- Contralateral invasive breast cancer
- Secondary primary cancer (not breast cancer)
- Death from any cause

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

For the "recurrence rate" and "disease-free survival" endpoint components of the "recurrences" endpoint, there was a statistically significant difference in each case to the advantage of abemaciclib in combination with endocrine therapy compared to endocrine therapy.

Overall analysis of both endpoint components showed a relevant, yet minor, advantage of abemaciclib in combination with endocrine therapy in terms of preventing recurrences.

Symptomatology (FACIT-Fatigue)

In the MONARCH-E study, the endpoint of symptomatology was assessed using the validated survey instrument FACIT-Fatigue.

In the dossier, the pharmaceutical company submitted analyses of the course and change of symptomatology from baseline using a mixed model for repeated measures (MMRM). However, there are discrepancies in the data on the number of female patients included in the respective analyses at individual survey time points. Furthermore, no data on the total number of female patients are available. Given the patient numbers indicated for each measurement time point in the tabulated changes from baseline, the MMRM analyses were assumed to include a sufficient number of patients and were therefore used despite the limitations mentioned.

For the endpoint of symptomatology, there was a statistically significant difference to the disadvantage of abemaciclib in combination with endocrine therapy. However, it cannot be inferred that the observed effect is relevant as the 95% CI of the standardised mean difference does not lie entirely outside the irrelevance range of –0.2 to 0.2.

Health status (EQ-5D VAS)

The health status was assessed using the visual analogue scale of the EQ-5D questionnaire.

For the endpoint of health status, the pharmaceutical company provided the dossier with MMRM analyses of the course and change of symptomatology from baseline. For the symptomatology endpoint (FACIT-Fatigue) as already explained above, these MMRM analyses are used for the benefit assessment.

As a result, for the endpoint of health status, there was a statistically significant difference to the disadvantage of abemaciclib in combination with endocrine therapy. However, it cannot be inferred that the observed effect is relevant as the 95% CI of the standardised mean difference does not lie entirely outside the irrelevance range of –0.2 to 0.2.

In summary, in the endpoint category of morbidity, there was a relevant, yet minor, advantage in terms of preventing recurrences. With regard to symptomatology and health status, there were statistically significant differences to the disadvantage of abemaciclib in combination with endocrine therapy. However, it cannot be inferred that the observed effects are relevant. In the endpoint category of morbidity, an overall advantage of abemaciclib in combination with endocrine therapy was therefore observed.

Quality of life

Functional Assessment of Cancer Therapy – Endocrine Symptoms (FACT-ES)

The FACT-ES comprises the FACT-G scales and the endocrine symptom scale ESS-19, for which a total score is to be calculated. However, the pharmaceutical company only submitted the results of the subscale ESS-19 for the analysis of the FACT-ES. The additionally presented ESS-18 subscale corresponds to the ESS-19 scale with the final question omitted. This analysis also fails to comply with the guidelines for evaluating the FACT-ES.

The ESS-19 and ESS-18 are not used for the benefit assessment.

Functional Assessment of Cancer Therapy – Breast (FACT-B)

Health-related quality of life is also assessed in the study using the disease-specific FACT-B questionnaire. The FACT-B questionnaire consists of the cross-tumour disease questionnaire (FACT-G) and a breast cancer-specific subscale (BCS). Only the FACT-B total score is included in the assessment of the additional benefit as it comprehensively considers the data on the health-related quality of life of the patients.

The pharmaceutical company provided the FACT-B dossier with MMRM analyses of the course and change in the health-related quality of life from baseline. For the symptomatology endpoint (FACIT-Fatigue) as already explained above, these MMRM analyses are used for the benefit assessment.

For the endpoint of health-related quality of life, there was a statistically significant disadvantage of abemaciclib in combination with endocrine therapy. However, it cannot be inferred that the observed effect is relevant as the 95% CI of the standardised mean difference does not lie entirely outside the irrelevance range of –0.2 to 0.2.

In summary, in the quality of life category, there was a statistically significant disadvantage of abemaciclib in combination with endocrine therapy. However, it cannot be inferred that the observed effect is relevant. Neither an advantage nor a disadvantage of abemaciclib in combination with endocrine therapy in terms of the health-related quality of life was thus observed.

Side effects

Adverse events (AEs)

In the MONARCH-E study, an adverse event was observed in 98% of the female patients in the intervention arm and 89% of those 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 abemaciclib in combination with endocrine therapy compared to the control arm in each case.

Specific adverse events

For the specific AEs of skin and subcutaneous tissue disorders (AEs), vascular disorders (SAEs), blood and lymphatic system disorders (severe AEs), neutropenia (severe AEs), eye disorders (severe AEs), gastrointestinal disorders (severe AEs), diarrhoea (severe AEs), general disorders and administration site conditions (severe AEs), infections and infestations (severe AEs), physical examinations (severe AEs), metabolism and nutrition disorders (severe AEs), renal and urinary disorders (severe AEs) and respiratory, thoracic and mediastinal disorders (severe AEs), there was a statistically significant difference in each case to the disadvantage of abemaciclib in combination with endocrine therapy.

For the endpoint of musculoskeletal and connective tissue disorders (severe AEs), there was a significant difference to the advantage of abemaciclib in combination with endocrine therapy.

In summary, the disadvantages for the endpoints of SAEs, severe AEs and discontinuation due to AEs lead to an overall significant disadvantage of the treatment with abemaciclib in combination with endocrine therapy in terms of side effects. Detailed analysis also showed disadvantages in terms of the specific adverse events.

Overall assessment

Results on the endpoint categories of mortality, morbidity, health-related quality of life and side effects from the ongoing, open-label, randomised controlled trial MONARCH-E are available for the benefit assessment of abemaciclib in combination with endocrine therapy for the treatment of HR-positive, HER2-negative early breast cancer at high risk of recurrence in postmenopausal patients.

For the endpoint of overall survival, there was no statistically significant difference between the treatment groups.

In the endpoint category of morbidity, there was a relevant, yet minor, advantage of abemaciclib in combination with endocrine therapy in terms of preventing recurrences. In the present curative treatment setting, the prevention of recurrences is a very relevant therapeutic goal. For the endpoints of symptomatology (FACIT-Fatigue) and health status (EQ-5D VAS), there were statistically significant disadvantages of abemaciclib in combination with endocrine therapy. However, it cannot be inferred that the observed effects are relevant. An advantage of abemaciclib in combination with endocrine therapy was derived overall.

For the health-related quality of life (FACT-B), there was a statistically significant difference to the disadvantage of abemaciclib in combination with endocrine therapy. However, it cannot be inferred that the observed effect is relevant. Neither an advantage nor a disadvantage of abemaciclib in combination with endocrine therapy in terms of the health-related quality of life was thus observed.

With regard to side effects, an overall significant disadvantage of abemaciclib in combination with endocrine therapy can be observed due to the disadvantages for the endpoints of serious adverse events, severe adverse events and discontinuation due to AEs, as well as the specific AEs.

In the overall analysis, the relevant, yet minor, advantage in terms of recurrences was offset by significant disadvantages in terms of side effects. There was no statistically significant difference for the overall survival. In light of the absolute difference in recurrence events between the treatment groups, the G-BA concluded in a weighted decision that the significant disadvantages in terms of side effects call into question the relevant, yet minor, advantage for the endpoint of recurrences. In doing so, the limited reliability of the available results on

recurrences is taken into account, since censoring events occurred to a significant extent early on and then continuously throughout the study. It is therefore concluded that an additional benefit of abemaciclib in combination with endocrine therapy compared with endocrine therapy alone is not proven.

2.1.4 Summary of the assessment

The present assessment is the new benefit assessment of the active ingredient abemaciclib due to the expiry of the limitation of the resolution on 20.10.2022.

The therapeutic indication under assessment is as follows: Abemaciclib in combination with endocrine therapy is indicated for the adjuvant treatment of premenopausal and postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive early breast cancer at high risk of recurrence.

The following two patient groups

a1) premenopausal women with hormone receptor-positive, HER2-negative early breast cancer at high risk of recurrence and

a2) postmenopausal women with hormone receptor-positive, HER2-negative early breast cancer at high risk of recurrence

were reassessed.

The pharmaceutical company presented the results for the relevant sub-populations from the ongoing, open-label RCT MONARCH-E, which compared abemaciclib in combination with standard endocrine therapy versus standard endocrine therapy alone.

About patient group a1)

The appropriate comparator therapy was determined to be tamoxifen (if applicable, with additional ovarian function suppression) 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 ovarian function suppression (exemestane only in combination with triptorelin) or ribociclib in combination with an aromatase inhibitor.

For the overall survival, there was an advantage, which is rated overall as a relevant, yet minor, improvement.

With regard to morbidity, a relevant, yet minor, advantage in preventing recurrences was observed. For the symptomatology (FACIT-Fatigue), there was a statistically significant difference to the disadvantage of abemaciclib; however, it could not be concluded that the observed effect was relevant. There was no difference in terms of health status (EQ-5D VAS). Overall, an advantage was observed in terms of morbidity.

For the quality of life (FACT-B), there was a statistically significant difference to the disadvantage of abemaciclib; however, it could not be concluded that the observed effect was relevant. Consequently, neither an advantage nor a disadvantage was identified.

The disadvantages for the endpoints of SAEs, severe AEs and discontinuation due to AEs as well as the specific AEs lead to an overall significant disadvantage in terms of side effects.

In the overall analysis, the relevant, yet minor, advantage in terms of overall survival and recurrences was offset by significant disadvantages in terms of side effects. In a weighted decision, the G-BA concluded that there was a moderate – and not merely minor – improvement in treatment-related benefit and, consequently, a hint of a minor additional benefit for patient group a1).

About patient group a2)

The G-BA determined the appropriate comparator therapy 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) or ribociclib in combination with an aromatase inhibitor.

For overall survival, there was no difference between the treatment groups.

In the endpoint category of morbidity, there was a relevant, yet minor, advantage in terms of preventing recurrences. For the endpoints of symptomatology (FACIT-Fatigue) and health status (EQ-5D VAS), there were disadvantages but it could not be concluded that the observed effects were relevant. An advantage was observed overall.

For the health-related quality of life (FACT-B), there was a statistically significant difference to the disadvantage of abemaciclib; however, it could not be concluded that the observed effect was relevant. Therefore, neither an advantage nor a disadvantage could be observed.

The disadvantages for the endpoints of SAEs, severe AEs and discontinuation due to AEs as well as the specific AEs lead to an overall significant disadvantage in terms of side effects.

In summary, the relevant, yet minor, advantage in terms of recurrences was offset by significant disadvantages in terms of side effects. There was no statistically significant difference for the overall survival. In light of the absolute difference in recurrence events between the treatment groups, the G-BA concluded in a weighted decision that the significant disadvantages in terms of side effects call into question the relevant, yet minor, advantage for recurrences. In doing so, the limited reliability of the available results on recurrences is taken into account, since censoring events occurred to a significant extent early on and then continuously throughout the study. It is thus concluded that an additional benefit is not proven for patient group a2).

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. To calculate the number of female patients in the SHI target population, the pharmaceutical company applied the same methodology in the current procedure as that used in the dossier for the 1st procedure for abemaciclib in early breast cancer from 2022. The pre- and postmenopausal patient numbers estimated by the pharmaceutical company are still subject to almost identical uncertainties. In particular, with regard to the updated WHO data source used on the 5-year breast cancer prevalence from 2022[3], it remains unclear why the baseline population included patients who were mostly no longer eligible for adjuvant treatment with abemaciclib in combination with endocrine therapy. The patient numbers provided by the pharmaceutical company in the dossier are, for the most part, slightly higher than those in the first procedure. This is essentially due to a higher 5-year prevalence and the fact that the percentage of patients under observation following completion of adjuvant treatment has been multiplied by the number of patients with HR+ and HER2- breast cancer, which should be regarded as a partial correction.

[3] International Agency for Research on Cancer. Cancer Today: Estimated number of cases breast, both sexes, all ages [online]. 2024 [accessed: 25.09.2025]. URL: https://gco.iarc.fr/today/en/dataviz/pie-prevalence?mode=population&group_populations=0&types=2&prev_time=5&cancers=20.

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 Verzenios (active ingredient: abemaciclib) at the following publicly accessible link (last access: 4 June 2026):

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

Treatment with abemaciclib 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 from other specialist groups participating in the Oncology Agreement.

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 15 June 2026). The calculation of treatment costs is generally based on the last revised LAUER-TAXE® version following the publication of the benefit assessment.

Treatment period:

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

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

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

For postmenopausal women with HR-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 HR-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 HR-positive, HER2-negative, node-positive 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				

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Abemaciclib in combination with endocrine therapy				
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
Appropriate comparator therapy				
Tamoxifen (if applicable, with additional ovarian function suppression)				
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
Leuprorelin	1 x every 3 months	4.0	1	4.0
Olaparib as monotherapy or in combination with endocrine therapy (only female patients with germline BRCA1/2-mutations are eligible)				
Olaparib	Continuously, 2 x daily	365.0	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
Leuprorelin	1 x every 3 months	4.0	1	4.0
An aromatase inhibitor (anastrozole or letrozole or exemestane) in combination with ovarian function suppression (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
Ribociclib in combination with an aromatase inhibitor				

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
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

a2) Postmenopausal women with HR-positive, HER2-negative, node-positive 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				
Abemaciclib in combination with endocrine therapy				
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
Appropriate comparator therapy				
Aromatase inhibitor (anastrozole or letrozole) alone, or, if applicable, tamoxifen if aromatase inhibitors are unsuitable				
Tamoxifen	Continuously, 1 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
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 female patients with germline BRCA1/2-mutations are eligible)				

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Olaparib	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
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

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 comorbidities) are not taken into account when calculating the annual treatment costs.

a1) Premenopausal women with HR-positive, HER2-negative, node-positive 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					
Abemaciclib in combination with endocrine therapy					
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
Appropriate comparator therapy					
Tamoxifen (if applicable, with additional ovarian function suppression)					
Tamoxifen	20 mg	20 mg	1 x 20 mg	365.0	365 x 20 mg
If applicable, LHRH agonist					

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
Olaparib as monotherapy or in combination with endocrine therapy (only female patients with germline BRCA1/2-mutations are eligible)					
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 ovarian function suppression (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
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
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

a2) Postmenopausal women with HR-positive, HER2-negative, node-positive 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					

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Abemaciclib in combination with endocrine therapy					
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
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
Olaparib as monotherapy or in combination with endocrine therapy (only female patients with germline BRCA1/2-mutations are eligible)					
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
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

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 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					
Abemaciclib 150 mg	168 FCT	€ 6,068.30	€ 1.77	€ 343.27	€ 5,723.26
Anastrozole 1 mg[4]	100 FCT	€ 43.68	€ 1.77	€ 2.56	€ 39.35
Letrozole 2.5 mg[4]	120 FCT	€ 61.68	€ 1.77	€ 3.98	€ 55.93
Exemestane 25 mg[4]	100 FCT	€ 127.53	€ 1.77	€ 9.19	€ 116.57
Goserelin 3.6 mg	3 IMP	€ 681.20	€ 1.77	€ 37.09	€ 642.34
Triptorelin 3.75 mg	1 DSS	€ 236.80	€ 1.77	€ 28.53	€ 206.50
Leuprorelin 11.25 mg	2 SRM	€ 1,010.55	€ 1.77	€ 55.32	€ 953.46
Tamoxifen 20 mg[4]	100 TAB	€ 28.05	€ 1.77	€ 1.32	€ 24.96
Appropriate comparator therapy					
Anastrozole 1 mg[4]	100 FCT	€ 43.68	€ 1.77	€ 2.56	€ 39.35
Letrozole 2.5 mg[4]	120 FCT	€ 61.68	€ 1.77	€ 3.98	€ 55.93
Exemestane 25 mg[4]	100 FCT	€ 127.53	€ 1.77	€ 9.19	€ 116.57
Goserelin 3.6 mg	3 IMP	€ 681.20	€ 1.77	€ 37.09	€ 642.34
Triptorelin 3.75 mg	1 DSS	€ 236.80	€ 1.77	€ 28.53	€ 206.50
Leuprorelin 11.25 mg	2 SRM	€ 1,010.55	€ 1.77	€ 55.32	€ 953.46
Tamoxifen 20 mg[4]	100 TAB	€ 28.05	€ 1.77	€ 1.32	€ 24.96
Olaparib 100 mg	112 FCT	€ 3,138.43	€ 1.77	€ 175.94	€ 2,960.72
Ribociclib 200 mg	189 FCT	€ 6,846.14	€ 1.77	€ 0.00	€ 6,844.37
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.

[4] Fixed reimbursement rate

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 had to be taken into account.

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 6 October 2020, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

A review of the appropriate comparator therapy took place. At their session on 10 February 2026, the Subcommittee on Medicinal Products newly determined the appropriate comparator therapy.

On 27 February 2026, the pharmaceutical company submitted a dossier for the benefit assessment of abemaciclib to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 5 VerfO.

By letter dated 2 March 2026 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 abemaciclib.

The dossier assessment by the IQWiG was submitted to the G-BA on 28 May 2026, and the written statement procedure was initiated with publication on the G-BA website on 1 June 2026. The deadline for submitting written statements was 22 June 2026.

The oral hearing was held on 6 July 2026.

By letter dated 8 July 2026, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by the IQWiG was submitted to the G-BA on 31 July 2026.

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

The evaluation of the written statements received and the oral hearing were discussed at the Subcommittee's session on 11 August 2026, and deliberation of the draft resolution was concluded.

At their session on 20 August 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	6 October 2020	Determination of the appropriate comparator therapy
Subcommittee on Medicinal Products	10 February 2026	New determination of the appropriate comparator therapy
Working group Section 35a	30 June 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	6 July 2026	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	14.07.2026; 04.08.2026	Consultation on the dossier assessment by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	11 August 2026	Concluding discussion of the draft resolution
Plenum	20 August 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 20 August 2026

Federal Joint Committee
in accordance with Section 91 SGB V

The Chair

Dr Optendrenk