Rucaparib
(ovarian cancer; maintenance treatment after first-line therapy)

Benefit assessment according to §35a SGB V[1]

EXTRACT

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[1] Translation of Sections I 1 to I 5 of the dossier assessment *Rucaparib (Ovarialkarzinom; Erhaltungstherapie nach Erstlinientherapie) – Nutzenbewertung gemäß § 35a SGB V*. Please note: This document was translated by an external translator and is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
Im Mediapark 8
50670 Köln
Germany

Phone: +49 221 35685-0
Fax: +49 221 35685-1
E-mail: berichte@iqwig.de
Internet: www.iqwig.de

Medical and scientific advice

- Volker Heilmann

IQWiG thanks the medical and scientific advisor for his contribution to the dossier assessment. However, the advisor was not involved in the actual preparation of the dossier assessment. The responsibility for the contents of the dossier assessment lies solely with IQWiG.

Patient and family involvement

No feedback was received in the framework of the present dossier assessment.

IQWiG employees involved in the dossier assessment

- Stefanie Reken
- Christiane Balg
- Merlin Bittlinger
- Ulrike Lampert
- Ana Liberman
- Jona Lilienthal
- Katrin Nink
- Carolin Weigel

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Part I: Benefit assessment

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[2] Table numbers start with “2” as numbering follows that of the full dossier assessment.

I List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
AE	adverse event
CTCAE	Common Terminology Criteria for Adverse Events
FIGO	Fédération Internationale de Gynécologie et d'Obstétrique
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
RCT	randomized controlled trial
SAE	serious adverse event
SGB	Sozialgesetzbuch (Social Code Book)

I 1 Executive summary of the benefit assessment

Background

In accordance with § 35a Social Code Book (SGB) V, the Federal Joint Committee (G-BA) has commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug rucaparib. The assessment is based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the "company"). The dossier was sent to IQWiG on 14 December 2023.

Research question

The aim of the present report was the assessment of the added benefit of rucaparib as monotherapy for the maintenance treatment of adult patients with advanced (Fédération Internationale de Gynécologie et d'Obstétrique [FIGO] stages III and IV) high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy in comparison with the appropriate comparator therapy (ACT).

The research question presented in Table 2 is derived from the ACT specified by the G-BA.

Table 2: Research question of the benefit assessment of rucaparib

Therapeutic indication	**ACT[a]**
Maintenance treatment of adult patients with advanced (FIGO stages III and IV) high-grade epithelial ovarian cancer[b] who are in response (complete or partial) following completion of first-line platinum-based chemotherapy	Individualized treatment[c,d] selected from: bevacizumab olaparib niraparib olaparib in combination with bevacizumab

a. Presented is the ACT specified by the G-BA.
b. This term also includes fallopian tube and primary peritoneal cancer.
c. Taking into account the previous therapy, the presence of a BRCA 1/2 mutation, and the presence of genomic instability.
d. According to G-BA, for the implementation of individualized therapy in a study of direct comparison, the investigator is expected to have a selection of several treatment options at disposal to permit an individualized treatment decision taking into account the listed criteria (multicomparator study). A rationale must be provided for the choice and any limitation of treatment options. The decision on individualized treatment with regard to the comparator therapy should be made before group allocation (e.g. randomization). This does not apply to necessary therapy adjustments during the course of the study (e.g. due to the onset of symptoms or similar reasons). If only a single-comparator study is submitted, the extent to which conclusions on a subpopulation can be derived will be examined as part of the benefit assessment.
According to G-BA, olaparib as monotherapy and niraparib with regard to the previous therapy are considered appropriate treatment options as part of the individualized treatment designated as ACT following a previous first-line platinum-based chemotherapy without bevacizumab.

ACT: appropriate comparator therapy; BRCA: breast cancer susceptibility gene; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; G-BA: Federal Joint Committee

In the present dossier assessment, the term “ovarian cancer” includes ovarian, fallopian tube, and primary peritoneal cancer.

The company followed the G-BA's specification of the ACT.

The assessment is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. Randomized controlled trials (RCTs) are used to derive added benefit. This concurs with the company’s inclusion criteria.

Results

In line with the company’s assessment, the check of completeness of the study pool did not identify any relevant study for assessing the added benefit of rucaparib in comparison with the G-BA’s ACT. The company also does not identify any studies that it considers suitable for conducting indirect comparisons.

Overall, no suitable data are available in the dossier for the present benefit assessment.

Results on added benefit

Since no suitable data are available for the benefit assessment, there is no hint of an added benefit of rucaparib in comparison with the ACT; an added benefit is therefore not proven.

Table 3 presents a summary of the probability and extent of the added benefit of rucaparib.

Table 3: Rucaparib – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Maintenance treatment of adult patients with advanced (FIGO stages III and IV) high-grade epithelial ovarian cancer[b] who are in response (complete or partial) following completion of first-line platinum-based chemotherapy	Individualized treatment[c,d] selected from: bevacizumab olaparib niraparib olaparib in combination with bevacizumab	Added benefit not proven

a. Presented is the ACT specified by the G-BA.
b. This term also includes fallopian tube and primary peritoneal cancer.
c. Taking into account the previous therapy, the presence of a BRCA 1/2 mutation, and the presence of genomic instability.
d. According to G-BA, for the implementation of individualized therapy in a study of direct comparison, the investigator is expected to have a selection of several treatment options at disposal to permit an individualized treatment decision taking into account the listed criteria (multicomparator study). A rationale must be provided for the choice and any limitation of treatment options. The decision on individualized treatment with regard to the comparator therapy should be made before group allocation (e.g. randomization). This does not apply to necessary therapy adjustments during the course of the study (e.g. due to the onset of symptoms or similar reasons). If only a single-comparator study is submitted, the extent to which conclusions on a subpopulation can be derived will be examined as part of the benefit assessment.
According to G-BA, olaparib as monotherapy and niraparib with regard to the previous therapy are considered appropriate treatment options as part of the individualized treatment designated as ACT following a previous first-line platinum-based chemotherapy without bevacizumab.

ACT: appropriate comparator therapy; BRCA: breast cancer susceptibility gene; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; G-BA: Federal Joint Committee

The G-BA decides on the added benefit.

I 2 Research question

The aim of the present report was the assessment of the added benefit of rucaparib as monotherapy for the maintenance treatment of adult patients with advanced (FIGO Stages III and IV) high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy in comparison with the ACT.

The research question presented in Table 4 is derived from the ACT specified by the G-BA.

Table 4: Research question of the benefit assessment of rucaparib

Therapeutic indication	**ACT**[a]
Maintenance treatment of adult patients with advanced (FIGO stages III and IV) high-grade epithelial ovarian cancer[b] who are in response (complete or partial) following completion of first-line platinum-based chemotherapy	Individualized treatment[c,d] selected from: bevacizumab olaparib niraparib olaparib in combination with bevacizumab
a. Presented is the ACT specified by the G-BA. b. This term also includes fallopian tube and primary peritoneal cancer. c. Taking into account the previous therapy, the presence of a BRCA 1/2 mutation, and the presence of genomic instability. d. According to G-BA, for the implementation of individualized therapy in a study of direct comparison, the investigator is expected to have a selection of several treatment options at disposal to permit an individualized treatment decision taking into account the listed criteria (multicomparator study). A rationale must be provided for the choice and any limitation of treatment options. The decision on individualized treatment with regard to the comparator therapy should be made before group allocation (e.g. randomization). This does not apply to necessary therapy adjustments during the course of the study (e.g. due to the onset of symptoms or similar reasons). If only a single-comparator study is submitted, the extent to which conclusions on a subpopulation can be derived will be examined as part of the benefit assessment. According to G-BA, olaparib as monotherapy and niraparib with regard to the previous therapy are considered appropriate treatment options as part of the individualized treatment designated as ACT following a previous first-line platinum-based chemotherapy without bevacizumab. ACT: appropriate comparator therapy; BRCA: breast cancer susceptibility gene; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; G-BA: Federal Joint Committee	

According to the S3 guideline “Diagnostics, Therapy and Follow-up of Malignant Ovarian Tumours”, cancers of the ovaries, fallopian tubes, and peritoneum are jointly classified in case of the same pathogenesis and histomorphology [1]. In the present dossier assessment, the term “ovarian cancer” therefore includes ovarian, fallopian tube and peritoneal cancer.

The company followed the G-BA's specification of the ACT.

The assessment is conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. RCTs are used to derive added benefit. This concurs with the company’s inclusion criteria.

I 3 Information retrieval and study pool

The study pool of the assessment was compiled on the basis of the following information:

Sources of the company in the dossier:

- study list on rucaparib (status: 14 November 2023)
- bibliographical literature search on rucaparib (last search on 2 November 2023)
- search in trial registries/trial results databases for studies on rucaparib (last search on 14 November 2023)
- search on the G-BA website for rucaparib (last search on 20 November 2023)
- bibliographical literature search on ACTs (last search on 2 November 2023)
- search in trial registries/trial results databases for studies on ACTs (last search on 14 November 2023)
- search on the G-BA website for ACTs (last search on 20 November 2023)

To check the completeness of the study pool:

- search in trial registries for studies on rucaparib (last search on 27 December 2023); for search strategies, see I Appendix A of the full dossier assessment

In agreement with the company, the check of completeness of the study pool did not identify any relevant study for assessing the added benefit of rucaparib in comparison with the G-BA's ACT.

In the dossier, however, the company supportively presented the study ATHENA-MONO [2], in which rucaparib is compared to placebo. Since there was no comparison with the ACT, the study ATHENA-MONO, in agreement with the company, is assessed as unsuitable for the assessment of the added benefit of rucaparib in the present therapeutic indication.

Furthermore, the company conducted research for indirect comparisons. The company looked for RCTs eligible for an indirect comparison with rucaparib using the bridging comparator placebo. In doing so, it only considered the options of the ACT olaparib and niraparib. However, it did not look for bevacizumab as monotherapy or in combination with olaparib.

Through its information retrieval, the company identified the studies SOLO-1 (olaparib vs. placebo) and PRIMA (niraparib vs. placebo). The company considered both studies to be unsuitable for conducting an indirect comparison in the present research question. It justified this with the lack of implementation of the G-BA's ACT and insufficient comparability of the study populations on both sides of the indirect comparison. Thus, for the present assessment, neither results from directly comparative studies nor from indirect comparisons are available.

I 4 Results on added benefit

No suitable data are available for the assessment of rucaparib as monotherapy for the maintenance treatment of adult patients with advanced (FIGO Stages III and IV) high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy in comparison with the ACT. This results in no hint of an added benefit of rucaparib in comparison with the ACT. An added benefit is therefore not proven.

Probability and extent of added benefit, patient groups with therapeutically important added benefit[3]

The result of the assessment of the added benefit of rucaparib in comparison with the ACT is summarized in Table 5.

[3] On the basis of the scientific data analysed, IQWiG draws conclusions on the (added) benefit or harm of an intervention for each patient-relevant outcome. Depending on the number of studies analysed, the certainty of their results, and the direction and statistical significance of treatment effects, conclusions on the probability of (added) benefit or harm are graded into 4 categories: (1) “proof”, (2) “indication”, (3) “hint”, or (4) none of the first 3 categories applies (i.e., no data available or conclusions 1 to 3 cannot be drawn from the available data). The extent of added benefit or harm is graded into 3 categories: (1) major, (2) considerable, (3) minor (in addition, 3 further categories may apply: non-quantifiable extent of added benefit, added benefit not proven, or less benefit). For further details see [3,4].

Table 5: Rucaparib – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Maintenance treatment of adult patients with advanced (FIGO stages III and IV) high-grade epithelial ovarian cancer[b] who are in response (complete or partial) following completion of first-line platinum-based chemotherapy	Individualized treatment[c,d] selected from: bevacizumab olaparib niraparib olaparib in combination with bevacizumab	Added benefit not proven

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b. This term also includes fallopian tube and primary peritoneal cancer.
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ACT: appropriate comparator therapy; BRCA: breast cancer susceptibility gene; FIGO: Fédération Internationale de Gynécologie et d'Obstétrique; G-BA: Federal Joint Committee

The assessment described above concurs with that by the company.

The G-BA decides on the added benefit.

I 5 References for English extract

Please see full dossier assessment for full reference list.

The reference list contains citations provided by the company in which bibliographical information may be missing.

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The full report (German version) is published under https://www.iqwig.de/en/projects/a23-134.html.