Cancer Drugs Fund

Managed Access Agreement

Rucaparib for maintenance treatment of relapsed platinum-sensitive ovarian, fallopian tube or peritoneal cancer [TA611]

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Rucaparib for maintenance treatment of recurrent platinum-sensitive epithelial ovarian, fallopian tube and peritoneal cancer that has responded to platinum-based chemotherapy [TA611]

Company name: Clovis Oncology

Primary source of data collection: Ongoing clinical study (ARIEL3)

Secondary source of data collection: Public Health England routine population-wide cancer data sets, including Systemic Anti-Cancer Therapy data set

NICE Agreement Manager	Brad Groves, Associate Director, Managed Access
NHS England Agreement Manager	Prof Peter Clark, CDF Clinical Lead
Public Health England Agreement Manager	Martine Bomb, Head of Data Projects
Clovis Oncology Agreement Manager	Josh Bedel Senior Director, Pricing and Market Access - Europe

1 Purpose of data collection arrangement

1.1 The purpose of the agreement is to describe the arrangements and responsibilities for further data collection for rucaparib for maintenance treatment of recurrent platinum-sensitive epithelial ovarian, fallopian tube and peritoneal cancer that has responded to platinum-based chemotherapy [TA611]. A positive recommendation within the context of a managed access agreement has been decided by the appraisal committee.

2 Commencement and period of agreement

2.1 This data collection arrangement shall take effect on publication of the managed access agreement. The data collection period is anticipated to conclude in December 2021, when final overall survival data from the pivotal ARIEL3 trial are expected to be available (see Section 5). The process for exiting the Cancer Drugs Fund will begin at this point and the review of the NICE guidance will start.

2.2 As part of the managed access agreement, the technology will continue to be available through the Cancer Drugs Fund after the data collection period has ended and while the guidance is being reviewed. This assumes that the data collection period ends as planned and the review of guidance follows the standard timelines described in the addendum to NICE's methods and processes when appraising cancer technologies.

2.3 Any changes to the terms or duration of any part of the managed access agreement must be approved by NICE and NHS England as co-signatories to the agreement.

2.4 If data collection is anticipated to conclude earlier than the timelines stated in the managed access agreement, for example due to earlier than anticipated reporting of an ongoing clinical trial:

- Where capacity allows NICE will endeavour to reschedule the CDF guidance review date to align with the earlier reporting timelines.
- It may be necessary to amend the content of the final SACT or real-world data report (for example if planned outcomes will no longer provide meaningful data).

2.5 If data collection from an ongoing clinical trial is anticipated to be delayed, please note:

- Resource/capacity issues will not be accepted as reasons for delaying the associated CDF guidance review.

- Unless a strong compelling rationale is provided, the CDF guidance review will proceed according to the original timelines outlined in the managed access agreement.
- It may not be possible to amend the date of the final SACT or real-world data report, in which case it will be available before the Clinical Study report is completed.

3 Patient eligibility

3.1 Rucaparib has been recommended for use in the Cancer Drugs Fund as an option for maintenance treatment of relapsed, platinum-sensitive high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer that has responded to platinum-based chemotherapy in adults only if the conditions in the managed access agreement for rucaparib are followed.

3.2 The NHSE Blueteq form define the patient eligibility criteria. There are 2 forms, one for BRCA mutated and one for non-BRCA mutated. The key patient eligibility criteria for the use of rucaparib in the Cancer Drugs Fund include (it is indicated where the criteria are only for the BRCA mutated* and the non-BRCA mutated**)[1]:

- Application is made by and the first cycle of systemic anti-cancer therapy with rucaparib will be prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy.
- Patient has a proven histological diagnosis of predominantly high grade serous or endometrioid ovarian, fallopian tube or primary peritoneal carcinoma
- Patient has had germline and/or somatic (tumour) BRCA testing.

[1] There criteria are indicative of the Blueteq criteria provide by NHS England. For the definitive criteria please see the CDF list on the NHS England website https://www.england.nhs.uk/cancer/cdf/cancer-drugs-fund-list/.

- *I confirm that this patient HAS a documented deleterious or suspected deleterious BRCA mutation(s) in the germline or in the tumour or in both. Please enter below the type of testing done in this patient to determine the presence of deleterious or suspected deleterious BRCA mutation(s):
    - in the germline only, or
    - in the tumour (somatic tissue) only, or
    - in both germline and somatic tissue
- *Patient HAS a documented deleterious or suspected deleterious BRCA 1 or BRCA 2 mutation(s), specify:
    - BRCA 1 mutation, or
    - BRCA 2 mutation, or
    - both BRCA1 and BRCA 2 mutations
- **Patient DOES NOT HAVE a documented deleterious or suspected deleterious BRCA mutation(s) in the germline or in the tumour.
- Patient had disease which was sensitive to the penultimate line of platinum-based chemotherapy (ie the disease responded to the line of platinum-based chemotherapy preceding the most recent line of platinum-based chemotherapy).
- Patient has recently completed a further line of platinum-based chemotherapy and has received a minimum of 4 cycles of platinum-based treatment. Specify:
    - 2nd line, or
    - 3rd line, or

  - 4th line or greater

- Patient has responded to the recently completed SECOND or subsequent line platinum-based chemotherapy platinum- based chemotherapy and has achieved a partial or complete response to treatment according to the definitions given below and with no evidence of progressive disease on the post-treatment scan or a rising CA125 level. Please specify which response assessment applies to this patient:

  - achieved a complete response at the end of the recent 2nd or subsequent line platinum-based chemotherapy ie has no measurable or non-measurable disease on the post-chemotherapy scan and the CA125 is normal, or

  - achieved a partial response at the end of the recent 2nd or subsequent line platinum-based chemotherapy ie has had a ≥30% reduction in measurableor non-measurable disease from the start of to the completion of the 2nd platinum-based chemotherapy or the patient has a complete remission on the post-chemotherapy CT scan but the CA125 has not decreased to within the normal range

- Patient is currently less than 8 weeks from the date of the last infusion of the last cycle of the 2nd or subsequent line of platinum-based chemotherapy.

- Patient has not previously received any PARP inhibitor unless niraparib via the CDF has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression or olaparib tablets via the CDF in the relapsed setting and the patient meets all the other criteria listed here. specify:

  - the patient has never previously received a PARP inhibitor, or
  - the patient has previously received niraparib via the CDF and this has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression
  - the patient has previously received rucaparib via an early access scheme and the patient meets all the other criteria listed here

- Rucaparib will be used as monotherapy.
- Patient has an ECOG performance status of either 0 or 1.
  - Note: a patient with a performance status of 2 or more is not eligible for rucaparib
- Rucaparib is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment.
- A formal medical review as to whether maintenance treatment with rucaparib should continue or not will be scheduled to occur at least by the start of the third cycle of treatment.
- No treatment breaks of more than 6 weeks beyond the expected cycle length are allowed (to allow any toxicity of current therapy to settle or intercurrent comorbidities to improve).
- Rucaparib is to be otherwise used as set out in its Summary of Product Characteristics

3.3 Rucaparib has been available for the maintenance treatment of adult patients with platinum-sensitive relapsed high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or

partial) to platinum-based chemotherapy through a Clovis Oncology initiated rucaparib early access programme (RAP) since March 2018. This programme has provided access to rucaparib maintenance for patients who in the opinion of their treating physician, had an unmet need that could not be met by existing approved and commercially available drugs.

3.4 Based on the final Budget Impact Analysis agreed with NICE, the company expects to treat an estimated [redacted] in total for the period until December 2021 within the Cancer Drugs Fund across the population outlined in Section 3.1 of this document.

3.5 In line with the final Budget Impact Analysis agreed with NICE, it is estimated the average treatment duration to be [redacted] for the population outlined in Section 3.1 of this document. Similarly, based on the final cost-effectiveness model submitted to NICE, the company estimates the overall survival for the population to be 4.919 years.

4 Area(s) of clinical uncertainty

4.1 The clinical uncertainty associated with rucaparib is due to the immaturity of the overall survival data currently available; this will be addressed through the collection of additional data from ARIEL3 (see Section 5).

5 Source(s) of data collection

Clinical trial

5.1 The primary source of data collection during the managed access agreement period will be the ongoing ARIEL3 trial: a randomised, international, double-blind, placebo-controlled, multicentre, Phase III study evaluating rucaparib versus placebo as maintenance therapy in recurrent, platinum-sensitive ovarian cancer.

5.2 The ARIEL3 trial met its primary endpoint by demonstrating a significant and clinically meaningful improvement in progression free survival for the

intention to treat population (ITT). The final overall survival analyses will be conducted at 70% maturity (estimated data cut-off [redacted]).

Other data

5.3 NHS England's Blueteq database captures the CDF population. NHS England shares Blueteq data with Public Health England for the CDF evaluation purposes. That sharing is governed by a data sharing agreement between NHS England and Public Health England.

5.4 Public Health England identifies, collects, collates, quality-assures and analyses large population-level datasets for specific diseases and conditions, including cancer. These datasets include the Systemic Anti-cancer Therapy (SACT) dataset, which is a mandated dataset as part of the Health and Social Care Information Standards. Public Health England will use the routinely-captured data collected during the period of the data collection arrangement to provide analyses defined in Sections 6.2 and 7.3.

5.5 Public Health England will collect data, including via the SACT dataset, alongside the primary source of data collection.

5.6 Patients who are receiving rucaparib maintenance treatment through the company's RAP and meet the patient eligibility criteria for the use of rucaparib in the Cancer Drugs Fund will be considered for inclusion in the Cancer Drugs Fund, subject to agreement with NHS England, but these patients will not be included in the data collection.

6 Outcome data

Clinical trial

6.1 Final overall survival data from ARIEL3 will provide an additional [redacted] follow-up relative to the evidence presented in NICE appraisal TA611 (15 April 2017 data cut-off) and should address clinical uncertainty regarding the long-term survival benefit of rucaparib maintenance treatment in the population covered by this managed access agreement.

Other data, including SACT

6.2 Data will be collected via Public Health England's routine population-wide datasets, including the SACT dataset. This collection will support data collected in the clinical trial. During the managed access agreement period, Public Health England will collect data to provide information on overall survival, duration of therapy, type of subsequent therapy (i.e. drug/regimen name) and time to subsequent therapy (if available) unless it is determined by the SACT Operational Group that no meaningful data will be captured in during the period of data collection.

7 Data analysis plan

Clinical trials

7.1 In accordance with the statistical analysis plan for ARIEL3, the final analysis of overall survival will occur when 70% of patients have died (estimated data cut-off [redacted]).

7.2 There will be no interim analysis for overall survival. Any revisions in the timing of the final overall survival analyses will be communicated with NICE and NHSE.

Other data

7.3 At the end of the data collection period Public Health England will provide a final report for NHS England based on routinely collected population-wide data, including that collected via SACT. The report will present depersonalised summary data, including the total number of patients starting treatment, overall survival, treatment duration, next subsequent treatment type (i.e. drug/regimen name) and time to next first subsequent treatment (if available). The necessary controls will be put in place to ensure that patient confidentiality is not put at risk. The report will be shared with Clovis Oncology in advance of the planned review of guidance.

7.4 Completeness of SACT dataset reporting will be shared with NHS England and Clovis Oncology at regular intervals during the data collection period. Public Health England will provide summary results for time on treatment and survival to NHS England and Clovis Oncology on an annual basis, to check the continuing validity of the period of the data collection arrangement. The final report from PHE will automatically part of NHS England submission to the CDF review.

8 Ownership of the data

8.1 Clovis Oncology will be the owner of all ARIEL3 trial data.

8.2 No additional governance arrangements are required as data will be collected through the ongoing ARIEL3 trial and routine Public Health England data collection.

8.3 The data analysed by Public Health England is derived from patient-level information collected by the NHS, as part of the care and support of cancer patients. The data is collated, maintained, quality-assured and analysed by the National Cancer Registration and Analysis Service, which is part of Public Health England. Access to the data was facilitated by the Public Health England Office for Data Release. Clovis Oncology will not have access to the Public Health England patient data, but will receive de-personalised summary data, with appropriate controls in place to cover this. Public Health England will provide a report to NHS England and Clovis Oncology at the end of the managed access period.

8.4 The SACT dataset is a mandated dataset as part of the Health and Social Care Information Standards. All necessary governance arrangements through SACT, and other datasets brought together by Public Health England, have been established with NHS Trusts and NHS England.

8.5 Blueteq's CDF system data is owned by NHS England. NHS England is responsible for implementing Blueteq data collection and generally for

analysis of these data. NHS England, however, shares Blueteq data with Public Health England for CDF evaluation purposes. That sharing is governed by a data sharing agreement between NHS England and Public Health England.

9 Publication

9.1 The details/authorship of any proposed publications arising from the ARIEL3 trial will be planned with the publication of the final study results.

9.2 Publication of the analysis results of data collected by Public Health England, including through SACT and the data from Blueteq's CDF system, will be planned and implemented by Public Health England.

10 Data protection

10.1 The terms of clause 7 (data protection) of the managed access agreement, as apply between NHS England and Clovis Oncology, shall also apply between the parties to this data collection arrangement in relation to the performance of their obligations under this data collection arrangement

11 Equality considerations

11.1 Do you think there are any equality issues raised in data collection?

☐ Yes ☒ No

Commercial Access Agreement

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The contents of this document have been redacted as they are confidential

- A glossary of terms relating to managed access agreements in the Cancer Drugs Fund is available here.