Cancer Drugs Fund

Managed Access Agreement

Niraparib for maintenance treatment of advanced ovarian, fallopian tube and peritoneal cancer after response to first-line platinum-based chemotherapy [TA673]

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Niraparib for maintenance treatment of advanced ovarian, fallopian tube and peritoneal cancer after response to first-line platinum-based chemotherapy [TA673]

Company name: GlaxoSmithKline

Primary source of data collection: Ongoing PRIMA clinical trial

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

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Public Health England Agreement Manager	Martine Bomb, Head of Data Projects
GlaxoSmithKline Agreement Manager	Nichola Roebuck, Medical Director Women's Cancer

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 niraparib as maintenance treatment of adult patients with advanced ovarian, fallopian tube and peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy [TA673]. A positive recommendation within the context of a managed access agreement (MAA) 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.

2.2 Estimated dates for data collection, reporting and submission for CDF guidance review are:

End of data collection (primary source)	[redacted]
Data available for development of company submission	[redacted]
Anticipated company submission to NICE for Cancer Drugs Fund review	March 2025

2.3 GSK anticipates that the results from the additional data collected during the Cancer Drugs Fund period will be incorporated into an evidence submission and the updated economic model by March 2025 to allow enough time for data analysis and cost-effectiveness analysis update.

2.4 GlaxoSmithKline acknowledges its responsibility to adhere as closely as possible to the timelines presented in the document.

2.5 NICE will, as far as is practicable, schedule a Cancer Drugs Fund review into the technology appraisal work programme to align with the estimated dates for the end of data collection. The review will use the process and methods in place at the time the invitation to participate in the guidance review is issued, which will be no earlier than 4 weeks prior to the anticipated company submission date. For further details of the

expected timelines for the Cancer Drugs Fund guidance review see 6.27 of the technology appraisal process guide.

2.6 As part of the managed access agreement, the technology will continue to be available through the Cancer Drugs Fund after the end of data collection and while the guidance is being reviewed. This assumes that the data collection period ends as planned and the review of guidance follows the Cancer Drugs Fund guidance review timelines described in NICE's guide to the processes of technology appraisal.

2.7 The company is responsible for paying all associated charges for a Cancer Drugs Fund review. Further information is available on the NICE website.

2.8 The company must inform NICE and NHS England and NHS Improvement of any anticipated changes to the estimated dates for data collection at the earliest opportunity.

2.9 Any changes to the terms or duration of any part of the data collection arrangement must be approved by NICE and NHS England and NHS Improvement.

2.10 If data collection is anticipated to conclude earlier than the estimated dates for data collection, for example due to earlier than anticipated reporting of an ongoing clinical trial, the company should note:

- Where capacity allows, NICE will explore options to reschedule the Cancer Drugs Fund 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 outputs will no longer provide meaningful data).

2.11 If data collection is anticipated to conclude later than the estimated dates for data collection, the company should note:

- The company must submit a written request to NICE and NHS England and NHS Improvement, with details of the extension requested, including an explanation of the factors contributing to the request.
- It may be necessary for the company to mitigate the impact of any delay, and reduce any risks of further delays.
- In the event of an extension, it may not be possible to amend the date of the final SACT or real-world data report, although NICE will explore options with Public Health England to provide data over the extended period.

2.12 NICE and NHS England and NHS Improvement may consider the data collection agreement no longer valid, and withdraw the technology from the Cancer Drugs Fund for the following, non-exhaustive, grounds:

- The primary sources of data are delayed, without reasonable justification.
- The primary sources of data are unlikely to report outcome data that could resolve the uncertainties identified by the technology appraisal committee.
- Amendments are made to the marketing authorisation.

3 Patient eligibility

3.1 Key patient eligibility criteria for the use of niraparib in the Cancer Drugs Fund include:

- application is being made by and the first cycle of systemic anti-cancer therapy with niraparib 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.
- patient has recently diagnosed FIGO stage III or IV ovarian, fallopian tube or primary peritoneal carcinoma.
- confirmation that one of the following scenarios applies to the surgical management of the patient in relation to the stage of the disease:
    - the patient has stage III disease and had an upfront attempt at optimal cytoreductive surgery **and** had no visible residual diseasea at the end of surgery **or**
    - the patient has stage III disease and had an upfront attempt at optimal cytoreductive surgery **and** had visible residual disease at the end of surgery **or**
    - the patient has stage III disease and had an interval attempt at optimal cytoreductive surgery **or**
    - the patient has stage IV disease and had an upfront attempt at optimal cytoreductive surgery **or**
    - the patient has stage IV disease and had an interval attempt at optimal cytoreductive surgery **or**
    - the patient has stage IV disease and has had a biopsy only
- patient has been treated with platinum-based 1st line chemotherapy and has received a minimum of 4 cycles of platinum-based treatment.

- patient has responded to the recently completed 1st line 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.

    - achieved a complete response at the end of 1st line 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 1st line chemotherapy ie has had a ≥30% reduction in measurable or non-measurable disease from the start of to the completion of 1st line 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.

- confirmation that the patient will commence maintenance niraparib within 12 weeks from the date of the first day of the last cycle of 1st line chemotherapy, unless the patient was previously entered into the company's early access scheme for maintenance niraparib after 1st line chemotherapy and all the other treatment criteria on this form are fulfilled.

- If BRCA negative, confirmation that the patient has not previously received any PARP inhibitor unless the patient has received niraparib as part of a company early access scheme for this 1st line maintenance indication and all the criteria set out in this form are fulfilled, or if BRCA positive confirm that the patient has not previously received any PARP inhibitor unless either the patient has received niraparib as part of a company's early access scheme for this 1st line

maintenance indication and the patient meets all the other criteria set out in this form or 1st line maintenance olaparib 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.

- confirmation that niraparib will be used as monotherapy.
- confirmation that maintenance niraparib is not being administered concurrently with maintenance bevacizumab.
- patient has an ECOG performance status of either 0 or 1.
- confirmation that niraparib is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment, whichever is the sooner.
- recommended starting dose for niraparib is 200mg daily **unless** the patient weighs ≥77Kg **and** has a platelet count ≥150,000 x 10^9/uL in which case the recommended starting dose is 300mg daily.
- the marketing authorisation for niraparib recommends that full blood counts are performed weekly for the 1st month of treatment with niraparib, monthly for the 1st year of therapy and then periodically thereafter during drug treatment with niraparib.
- the marketing authorisation for niraparib recommends that the patient's blood pressure is monitored weekly for the first 2 months of treatment, monthly for the next 10 months of therapy and then periodically thereafter during drug treatment with niraparib.
- confirmation that a first formal medical review as to whether maintenance treatment with niraparib should continue or not will be scheduled to occur at least by the start of the third cycle of treatment.

- confirmation that when a treatment break of more than 6 weeks beyond the expected 4-weekly cycle length is needed, I will complete a treatment break approval form to restart treatment, including as appropriate if the patient had an extended break on account of Covid-19.

- confirmation that niraparib is to be otherwise used as set out in its Summary of Product Characteristics

3.2 Niraparib has been available for women with newly diagnosed advanced BRCA wildtype ovarian cancer through a company-sponsored early access programme since April 2020. The programme provides ethical access to niraparib for patients with newly diagnosed advanced ovarian cancer, who in their treating physicians' opinion, had an unmet clinical need that could not be treated with approved and commercially available drugs. The company enabled access to patients without a documented BRCA mutation only due to the availability of olaparib via the Cancer Drugs Fund for patients with BRCA mutations in the same 1st line maintenance indication.

3.3 As of November 2020, [redacted] people in England have received niraparib in this indication, via the company-sponsored early access programme. These patients will not be included as part of the SACT data collection agreement because baseline characteristics were not collected and they may not be comparable to those treated in within the Cancer Drugs Fund.

3.4 The estimated patient numbers per year for this technology within the Cancer Drugs Fund are:

As estimated by the company	[redacted]

As estimated by NICE Resource Impact Assessment team	[redacted]

4 Area(s) of clinical uncertainty

4.1 The appraisal committee identified the following key areas of uncertainty during the course of the appraisal process:

1. Immaturity of data concerning overall survival and time to second progression,
2. Long-term progression-free survival in people having the technology,
3. Generalisability of the clinical outcome data from the PRIMA trial to people with stage 3 no visible residual disease after primary debulking surgery

4.2 The committee concluded that further data collection within the Cancer Drugs Fund could resolve these uncertainties. For further details of the committee's discussion see section 3 of the Final Appraisal Document.

5 Sources of data collection

Primary and secondary sources of data collection

Primary source(s)	○ PRIMA trial
Secondary sources	○ Systemic Anti-Cancer Therapy (SACT) dataset ○ NHS England and NHS Improvement's Blueteq data

Description of sources

5.1 The PRIMA trial is a robust, high quality, randomised, double-blinded, placebo-controlled, multi-centre, phase 3 trial to assess the efficacy and safety of niraparib maintenance treatment for adult patients with advanced, high grade ovarian cancer who are in response (complete or

partial) following completion of first-line platinum-based chemotherapy. Patients were randomly assigned in a 2:1 ratio to receive either niraparib or placebo once daily.

5.2 NHS England and NHS Improvement's Blueteq database captures the Cancer Drugs Fund population. NHS England and NHS Improvement shares Blueteq data with Public Health England for the Cancer Drugs Fund evaluation purposes. That sharing is governed by a data sharing agreement between NHS England and NHS Improvement and Public Health England.

5.3 The Systemic Anti-Cancer Therapy (SACT) dataset, is a mandated dataset as part of the Health and Social Care Information Standards. Public Health England is responsible for the collection, collation, quality-assurance and analysis of this dataset.

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

6 Outcome data

Clinical trial

6.1 The most pertinent outcome to be measured is long-term overall survival (OS). The PRIMA final OS analysis will be event-driven and conducted at approximately 60% maturity (no interim analyses are planned for OS data). This is anticipated to be in [redacted] and will provide an additional 5 years follow up to the data cut used in committee decision making. The trial will also collect data on all of its outcomes including progression free survival (PFS) and progression free survival 2 (PFS2). This will be provided to NICE when the guidance is reviewed and will be supplemented by the data collected in SACT.

Other data, including SACT

6.2 Public Health England will collect the following outcomes through SACT unless it is determined by the SACT Operational Group that no meaningful data will be captured during the period of data collection:

- Number of patients starting treatment
- Baseline patient characteristics, including gender, age and performance status
- Treatment duration
- Time to first subsequent systemic anti-cancer treatment (if available)
- Overall survival
- The proportion of people having subsequent systemic anti-cancer treatment and the treatments used (if available)

6.3 NHS England and NHS Improvement's Blueteq system will collect the following outcomes:

- Number of applications to start treatment
- BRCA status
- FIGO stage
- Starting dose
- Type of debulking surgery (primary or interval)
- Presence of visible residual disease after primary debulking surgery in patients with stage III disease

7 Data analysis plan

Clinical trials

7.1 At the end of the data collection period, which is event-driven and conducted at approximately 60% OS data maturity, the final OS data from the PRIMA trial will be used to update the economic model. This is expected to provide an additional 5 years follow up to the data cut used in committee decision making.The final analysis will follow the analysis plan outlined in the trial protocol.

7.2 No interim analysis are planned for OS data.

7.3 Database lock is event driven, however it is anticipated to happen in [redacted]. Data will be analysed at that time.

Other data

7.4 At the end of the data collection period Public Health England will provide a final report for NHS England and NHS Improvement which provide analyses based on NHS England and NHS Improvement's Blueteq data and routinely collected population-wide data, including that collected via SACT. The necessary controls will be put in place to ensure that patient confidentiality is not put at risk. The report will be shared with the company in advance of the planned review of guidance. Where SACT is a secondary source of data, availability of the final SACT report will be aligned to the availability of data from the primary source. The end of SACT data collection will be 8 months prior to the availability of the final SACT report to allow for NHS trusts to upload SACT data, data cleaning, and report production.

8 Ownership of the data

8.1 For the PRIMA clinical trial data listed above, GlaxoSmithKline will be the owner.

8.2 No additional governance arrangements are required as data will be collected through on-going clinical trials and routine PHE 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 is facilitated by the Public Health England Office for Data Release. The company will not have access to the Public Health England patient data, but will receive de-personalised summary data, with appropriate governance controls in place.

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 and NHS Improvement.

8.5 Blueteq's Cancer Drugs Fund system data is owned by NHS England and NHS Improvement. NHS England and NHS Improvement is responsible for implementing Blueteq data collection and generally for the analysis of these data. NHS England and NHS Improvement, however, shares Blueteq data with Public Health England for Cancer Drugs Fund evaluation purposes. That sharing is governed by a data sharing agreement between NHS England and NHS Improvement and Public Health England.

9 Publication

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

9.2 Public Health England will produce a final report which includes analysis of data collected through SACT and from NHS England and NHS Improvement's Blueteq system. This report will be provided to NHS England and NHS Improvement and the company at the end of the managed access period. The final report will form part of NHS England and NHS Improvement's submission to the Cancer Drugs Fund guidance review, and will therefore be publicly available at the conclusion of guidance review.

9.3 Public Health England will produce interim reports, which will be shared with NHS England and NHS Improvement, NICE and the company at regular intervals during the data collection period. These reports will be used to determine whether real-world data collection is proceeding as anticipated, and will not form part of the guidance review.

9.4 Publications of any data from the Public Health England reports is not permitted until after the date of publication of the NICE committee papers (on the NICE website) following the first NICE guidance review committee meeting.

9.5 The contribution of all relevant individuals must be acknowledged in any publications regarding the data collection or analyses generated from the data collection arrangement. Authors will need to contact the NICE Managed Access Team for the full list of relevant individuals.

10 Data protection

10.1 The terms of clause 7 (data protection) of the managed access agreement, that apply between NHS England and NHS Improvement and GlaxoSmithKline, 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.