Managed Access Agreement

Dostarlimab for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (TA779)

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Dostarlimab for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (TA779)

Company name: GlaxoSmithKline

Primary source of data collection: Ongoing GARNET trial NCT02715284

Secondary source of data collection: NHS Digital routine population-wide cancer data sets, including Systemic Anti-Cancer Therapy data set

NICE Agreement Manager	Brad Groves, Associate Director, Managed Access
NHSE&I Agreement Manager	Prof Peter Clark, CDF Clinical Lead
NHS Digital Agreement Manager	Martine Bomb, Head of Data Projects
GlaxoSmithKline Agreement Manager	Claire Gait, Oncology Health Outcomes Director

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 dostarlimab for previously treated advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency [TA779]. 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	April 2025

2.3 GlaxoSmithKline anticipate 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 April 2025 to allow enough time for the data analysis and cost-effectiveness analysis to be updated.

2.4 GlaxoSmithKline acknowledge their responsibility to adhere as closely as possible to the timelines presented in this document.

2.5 NICE will, as far as is practicable, schedule a Cancer Drugs Fund review into the technology appraisal work program 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 (NHSE&I) in writing 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 NHSE&I.

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 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 NHSE&I, 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 NHS Digital to provide data over the extended period.

2.12 GlaxoSmithKline acknowledge their responsibility to provide an evidence submission for this technology to NICE under all circumstances following a period of managed access.

2.13 In the event that GlaxoSmithKline do not make a submission to NICE for the purpose of updating the guidance, NICE and NHSE&I will require the company to agree to submit the clinical evidence collected during the managed access period, and to participate in an engagement meeting convened by NICE with attendance from NHSE&I, patient and professional group stakeholders, with the company presenting the clinical evidence collected during the managed access period and an explanation of the decision to proceed with withdrawal of the guidance.

2.14 NICE and NHSE&I 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 dostarlimab in the Cancer Drugs Fund include:

- the application is being made by, and the first cycle of systemic anti-cancer therapy with dostarlimab will be prescribed by, a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy.
- the prescribing clinician is fully aware of the management of and the treatment modifications that may be required for immune-related adverse reactions due to anti-PD-1/PD-L1 treatments including pneumonitis, colitis, nephritis, endocrinopathies, hepatitis and skin toxicity.
- the patient has a proven histological diagnosis of endometrial carcinoma.
- the patient has recurrent or locally advanced or metastatic disease.
- the patient's tumour has a documented presence of microsatellite instability-high (MSI-H) or DNA mismatch repair deficiency (dMMR) confirmed by validated testing.
- the patient has progressive disease during or following previous platinum-based therapy for recurrent/locally advanced/metastatic endometrial carcinoma.
- the patient has an ECOG performance status (PS) of 0 or 1.

- the patient has no symptomatic brain or leptomeningeal metastases.
- the patient has not received any prior treatment with an anti-PD-1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody unless the patient has been treated with dostarlimab in a company early access scheme and all other treatment criteria on this form apply.
- dostarlimab will be administered as monotherapy as follows: dostarlimab 500mg given for a maximum of 4 cycles every 3 weeks and then dostarlimab 1000mg is continued every 6 weeks.
- dostarlimab will be stopped on disease progression or unacceptable toxicity or withdrawal of patient consent, whichever occurs first.

  Note: there is no stopping rule for dostarlimab in this endometrial carcinoma indication and hence patients continuing to benefit from dostarlimab after 2 years of treatment can continue if the patient and clinician agree.

  Note: once dostarlimab is stopped for disease progression or unacceptable toxicity or withdrawal of patient consent, dostarlimab cannot be re-started.
- a formal medical review as to whether treatment with dostarlimab should continue will occur at least by the end of the 2nd 3-weekly cycle of treatment.
- where a treatment break of more than 12 weeks beyond the expected 3- or 6-weekly cycle length is needed, a treatment break approval form will be completed to restart treatment, including indicating as

appropriate if the patient had an extended break because of COVID 19.

- dostarlimab will be otherwise used as set out in its Summary of Product Characteristics (SPCs).

3.2 An EAMs scheme is currently available. It has been operational since December 2020.

3.3 As of November 2021, [redacted] in England have received dostarlimab. These early access 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 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*	Year 1 – [redacted] Year 2 – [redacted] Year 3 - [redacted]
As estimated by NICE Resource Impact Assessment team	Year 1 – [redacted] Year 2 – [redacted] Year 3 - [redacted]

*Patient numbers based on v4 NHSE BIT

Patient safety

3.5 The company and NHSE&I have the responsibility to monitor the safety profile of the technology and must provide an overview of any new or updated safety concerns to NICE. If any new safety concerns are confirmed, NICE and NHSE&I will take steps, as appropriate, to mitigate

the risk including but not limited to updating the eligibility criteria or recommending that the managed access agreement be suspended.

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. Uncertainty about long-term survival given the immaturity of the data from GARNET.

2. Indirect comparisons of dostarlimab with other treatments are highly uncertain because of differences between the included studies.

4.2 The committee expects that at the point that the guidance is updated there will be further evidence available, specifically KEYNOTE-775, that will allow for a new matched adjusted treatment comparison to be presented.

4.3 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)	○ GARNET trial (cohort A1)
Secondary sources	○ Systemic Anti-Cancer Therapy (SACT) dataset ○ NHSE&I's Blueteq data

Description of sources

5.1 The GARNET trial is an open-label, single-arm, multicentre, non-randomised Phase I trial (NCT02715284). GARNET was conducted in two parts: Part 1 of the study, which established the recommended dose for dostarlimab (dose escalation). Part 2B (the extension phase) investigated the efficacy of dostarlimab in five expansion cohorts including dMMR/MSI-H EC, which was Cohort A1. Cohort A1 is the only cohort relevant to this technology appraisal and this DCA. The primary endpoints were overall response rate (ORR) and duration of response rate (DOR) based on blinded independent central review (BICR) using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1. The secondary endpoints were immune related disease control rate (irDCR), immune related DOR (irDOR), immune related PFS (irPFS), and Immune-related objective response rate (irORR) using irRECIST; PFS and DCR based on BICR using RECIST v1.1; OS, and immunogenicity.

5.2 NHSE&I's Blueteq database captures the Cancer Drugs Fund population. NHSE&I shares Blueteq data with NHS Digital for the Cancer Drugs Fund evaluation purposes. The lawfulness of this processing is covered under article 6(1)e of the United Kingdom General Data Protection Regulations (GDPR) (processing is necessary for the performance of a task carried out in the public interest or in the exercise of official authority vested in the controller). NHS Digital, through the National Disease Registration Service, does have statutory authority to process confidential patient information (without prior patient consent) afforded through the National Disease Registries (NDRS) Directions 2021 issued to it by the Secretary of State for Health and Social Care, and has issued the NDRS Data Provision Notice under section 259 of the Health and Social Care Act 2012 regarding collection of the Blueteq data from NHSE&I.

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

5.4 NHS Digital 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. A CDF specific GARNET cohort A1 interim OS analysis will be conducted in 2024 and will provide an additional [redacted] follow up to the data cut used in decision making. The trial will also collect data on all of its outcomes including PFS, and time on treatment can be derived from trial variables. This will be provided to NICE when guidance is reviewed and will be supplemented by the data collection of other datasets, including SACT.

Other data, including SACT

6.2 NHS Digital 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
- Overall survival

6.3 NHSE&I's Blueteq system will collect the following outcomes:

- Number of applications to start treatment
- Number of prior platinum-based chemotherapies
- Baseline patient characteristics including histology, prior surgery and type of recurrent disease

6.4 It was discussed whether additional baseline characteristics could be collected by the NHSE&I's Blueteq system to support the indirect comparisons of dostarlimab with other treatments. These characteristics included grade at diagnosis and FIGO stage. It was determined that these baseline characteristics could not be included within the data collection.

7 Data analysis plan

Clinical trials

7.1 At the end of the data collection period, month, year, the OS, PFS and ToT data from the GARNET trial will be used to update the economic model. This is expected to provide an additional [redacted] follow up to the data cut used in committee decision making. The analysis will follow the analysis plan outlined in the trial protocol.

7.2 An interim analysis (IA3) is expected in [redacted]

7.3 Database lock for the CDF analysis will happen in [redacted]. Data will be analyzed at that time.

7.4 Updated indirect comparisons of the dostarlimab GARNET data versus comparator data, including available chemotherapy data from the KEYNOTE-775 trial, will be provided.

Other data

7.5 At the end of the data collection period NHS Digital will provide a final report for NHSE&I which provide analyses based on NHSE&I'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 GARNET cohort A1 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 NHS digital data collection.

8.3 This work uses data that has been provided by patients and collected by the NHS as part of their care and support. The data are collated, maintained and quality assured by the National Disease Registration Service, which is part of NHS Digital. The company will not have access to the NHS Digital 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 NHS Digital, have been established with NHS Trusts and NHSE&I.

8.5 Blueteq's Cancer Drugs Fund system data is owned by NHSE&I. NHSE&I is responsible for implementing Blueteq data collection and generally for the analysis of these data. NHSE&I, however, shares Blueteq data with NHS Digital for Cancer Drugs Fund evaluation purposes. The lawfulness of this processing is covered under article 6(1)e of the United Kingdom General Data Protection Regulations (UK GDPR) (processing is necessary for the performance of a task carried out in the public interest or in the exercise of official authority vested in the controller). NHS Digital, through the National Disease Registration Service, does have statutory authority to process confidential patient information (without prior patient consent) afforded through the National Disease Registries (NDRS) Directions 2021 issued to it by the Secretary of State for Health and Social Care. The lawfulness of NHS Digital's processing is covered under article 6(1)(c) of the UK GDPR – processing is necessary for compliance with a legal obligation to which the controller is subject (the NDRS Directions).

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

9.3 NHS Digital will produce interim reports, which will be shared with NHSE&I, 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 Reports from NHS Digital will form part of GlaxoSmithKline's submission to the Cancer Drugs Fund guidance review, and will therefore be publicly available at the conclusion of guidance review. At a minimum an annual report must be provided to NICE and NHSE&I to determine whether real-world data collection is proceeding as anticipated, but will not form part of the guidance review.

9.5 Publications of any data from the NHS Digital 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.

9.6 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 NHSE&I 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.