Managed Access Agreement

Dostarlimab with platinum-containing chemotherapy for treating primary advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency [ID3968]

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Dostarlimab with platinum-containing chemotherapy for treating primary advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (ID3968)

Company name: GlaxoSmithKline (UK) Limited

Primary source of data collection: RUBY-1 clinical trial

Secondary source of data collection: Systemic Anti-Cancer Therapy data set

NICE Agreement Manager	[redacted], Associate Director, Managed Access
NHSE Agreement Manager	[redacted], National Cancer Drugs Fund Clinical Lead
NHSE Agreement Manager	[redacted], Head of Data Projects
GSK Agreement Manager	[redacted]

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 with platinum-containing chemotherapy for treating primary advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency (ID3968) (to be updated with TA number after final guidance has been published). 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 a guidance update are:

End of data collection (primary source)	[redacted]
Data available for development of company submission	[redacted]
Anticipated company submission to NICE for a guidance update	September 2024

2.3 GSK anticipates 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 September 2024. Data cleaning is required post the data cut. Detailed data analysis and survival analysis will be completed immediately post availability of the data in [redacted], and resubmitted in an updated model within [redacted]. GSK acknowledges its responsibility to adhere as closely as possible to the timelines presented in this document.

2.4 NICE will, as far as is practicable, schedule the guidance update into the technology appraisal work programme to align with the estimated dates for the end of data collection.

2.5 The NICE guidance update will follow the process and methods applicable to guidance updates that are in place at the time the invitation to

participate in the guidance update is issued. These may be different from the process and methods applicable to guidance updates when this technology entered into the managed access agreement.

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 guidance update follows the standard timelines.

2.7 The company is responsible for paying all associated charges for a guidance update. Further information is available on the NICE website.

2.8 The company must inform NICE and NHS England (NHSE) 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.

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 guidance update 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 NHSE, 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 NHSE to provide data over the extended period.

2.12 GSK acknowledge its 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 GSK does not make a submission to NICE for the purpose of updating the guidance, NICE and NHSE 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, 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 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:

- Both the application for the technology is being made by and the first cycle of systemic anti-cancer therapy with dostarlimab in combination with carboplatin and paclitaxel 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 treatments including pneumonitis, colitis, nephritis, endocrinopathies, hepatitis, myocarditis and skin toxicity.
- The patient has a histologically- or cytologically-confirmed diagnosis of endometrial carcinoma (including clear cell and serous histologies). Note: patients with carcinosarcoma (Mixed Mullerian tumour) are eligible but otherwise uterine sarcomas of any kind are NOT eligible for dostarlimab in this indication.
- The patient's tumour has a documented presence of mismatch repair deficiency (dMMR) or microsatellite instability (MSI-H) confirmed by validated testing.
- Either the patient has a 1st recurrence of endometrial carcinoma after surgery or radiotherapy or chemoradiotherapy or has presented with primary locally advanced or metastatic endometrial carcinoma and in whichever scenario is not a candidate for any potentially curative treatment with surgery or radiotherapy or chemoradiotherapy.

- The patient has not previously received any systemic chemotherapy for the endometrial carcinoma or the only systemic therapy has been as neoadjuvant or adjuvant chemotherapy or chemoradiotherapy and the patient has progressed or recurred at least 6 months since the completion of such chemotherapy.
- Dostarlimab will be given in combination with carboplatin and paclitaxel unless there is a clear contraindication to the use of one or both of these cytotoxic agents. Note: in patients who suffer a severe allergic reaction to paclitaxel or carboplatin which necessitates discontinuation of the drug causing the severe allergy, use of dostarlimab can continue with carboplatin or paclitaxel in combination with whichever agent is considered appropriate by the clinician.
- Unless the patient is contraindicated from starting with carboplatin and/or paclitaxel, the patient will commence combination chemotherapy with carboplatin at a dose of AUC 5mg/ml/min and paclitaxel at 175mg/m², planned to be given 3-weekly and for a maximum of 6 cycles of chemotherapy.
- The patient has not received any prior antibody treatment which targets PD-1 or PD-L1 or PD-L2 or CD137 or OX40 or anti-cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) or.
- The patient will be treated with a fixed dose of dostarlimab 500mg every 3 weeks when in combination with the chemotherapy and then at a dose of 1,000mg every 6 weeks as monotherapy.
- Treatment with dostarlimab will be stopped at whichever of the following events occurs first: disease progression or loss of clinical benefit or unacceptable toxicity or withdrawal of patient consent or after a maximum of 3 calendar years measured from the date of first dostarlimab treatment.

- During the informed consenting process, the patient has been informed that the maximum duration of treatment with dostarlimab is after a maximum of 3 calendar years of treatment.
- The patient has an ECOG performance status (PS) of 0 or 1. Note: NHS England does not fund this combination in patients of ECOG PS 2.
- The patient has no symptomatically active brain metastases or leptomeningeal metastases.
- A formal medical review as to how dostarlimab and carboplatin and paclitaxel are being tolerated, and whether treatment with this combination should continue or not, will be scheduled to occur at least by the end of the first 6 weeks of treatment.
- When a treatment break of more than 12 weeks beyond the expected 3 or 6 weekly cycle length is needed, a treatment break approval form to restart treatment will be completed.
- Dostarlimab will be otherwise used as set out in its Summary of Product Characteristics (SPC).

3.2 An early access to medicines scheme was open from July 2023 until October 2023 (3 months). An EAMS+ has been open from October 2023 and is still open (4 months as of February 2023).

3.3 As of January 2024, [redacted] people in England have received dostarlimab. These early access patients will be included as part of the SACT data collection agreement because additional data collection from SACT (specifically survival outcomes) can supplement the data collection (e.g. baseline characteristics) collected via the EAMS.

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] eligible patients ([redacted] patients treated 2024) Year 2 – [redacted] eligible patients ([redacted] patients continuing treatment from year one, and [redacted] new patients treated in Feb-Sep 2025 year two) Year 3 – [redacted] eligible patients *Based on NICE BIT to company v2., with [redacted]% annual uptake for number of patients treated. Note only year one (2024) and 9 months of year two (Feb-Sep 2025) is applicable with expected resubmission in September 2024, and therefore expected CDF exit September 2025. .*
As estimated by NICE Resource Impact Assessment team	Year 1 – [redacted] Year 2 – [redacted] Year 3 – [redacted]

4 Patient safety

4.1 The company and NHSE 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 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.

5 Area(s) of clinical uncertainty

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

1. Longer term overall survival data

5.2 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.

6 Sources of data collection

Primary and secondary sources of data collection

Primary source(s)	○ RUBY-1 trial
Secondary sources	○ Systemic Anti-Cancer Therapy (SACT) dataset ○ NHSE's Blueteq data

Description of sources

6.1 RUBY-1 (NCT03981796) is a multicentre, randomised, double blinded, placebo-controlled Phase 3 study. The trial recruited female patients with primary stage III or stage IV endometrial cancer or first recurrent endometrial cancer, with a low potential for cure by radiation therapy or surgery alone or in combination (intention to treat [ITT] N=494) [dMMR/MSI-H n=118]. The trial investigated dostarlimab in combination with carboplatin paclitaxel (N=245) [n=53 dMMR/MSI-H] compared with Placebo in combination with carboplatin paclitaxel (N=249) [n=65 dMMR/MSI-H]. The primary outcomes are PFS by investigator assessment (IA PFS) and Overall survival (OS).

6.2 NHSE's Blueteq database captures the Cancer Drugs Fund population. 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). NHSE, through the National Disease Registration Service (NDRS), does have statutory authority to process confidential patient

information (without prior patient consent) afforded through the 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.

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

6.4 NDRS in NHSE will collect data, including via the SACT dataset, alongside the primary source of data collection

7 Outcome data

Clinical trial

7.1 Longer term overall survival data will be provided from the RUBY-1 clinical trial. This will address the uncertainty identified by the appraisal committee.

Other data, including SACT

7.2 NDRS in NHSE 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

7.3 NHSE's Blueteq system will collect the following outcomes:

- Number of applications to start treatment

8 Data analysis plan

Clinical trials

8.1 The second interim analysis (IA2) of the RUBY-1 trial data cut was completed on [redacted]. The dMMR/MSI-H subgroup, the population specific to this decision problem, is a predefined subgroup within this data. The IA2 data will provide additional OS data specifically for the dMMR/MSI-H subgroup (in addition to the overall trial population, which is not relevant to this decision problem). RUBY-1 is an event driven trial and IA2 has taken place as planned per study protocol, based on forecasted rate of OS events, outlined fully in supplementary appendix Mirza et al. 2023.

8.2 [redacted]

Other data

8.3 At the end of the data collection period NHSE will provide a final report which provide analyses based on NHSE'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 guidance update. 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.

9 Ownership of the data

9.1 For all clinical trial data listed above, GSK will be the owner

9.2 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 NHSE. The company will not have access to the NHSE patient data, but will receive de-personalised summary data, with appropriate governance controls in place.

9.3 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 NHSE, have been established with NHS Trusts and NHSE.

9.4 Blueteq's Cancer Drugs Fund system data is owned by NHSE. NHSE is responsible for implementing Blueteq data collection and generally for the analysis of these data. 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). NHSE, 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 NHSE'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).

10 Publication

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

10.2 NDRS will produce a final report which includes analysis of data collected through SACT and from NHSE's Blueteq system. This report will be provided to NHSE and the company at the end of the managed access period. The final report will form part of NHSE's submission to the guidance update, and will therefore be publicly available at the conclusion of the guidance update.

10.3 NDRS will produce interim reports, which will be shared with 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 update.

10.4 Publications of any data from the NDRS reports is not permitted until after the date of publication of the NICE committee papers (on the NICE website) following the first NICE guidance update committee meeting.

10.5 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.

11 Data protection

11.1 The terms of clause 7 (data protection) of the managed access agreement, that apply between NHSE and GSK, shall also apply between

the parties to this data collection arrangement in relation to the performance of their obligations under this data collection arrangement

12 Equality considerations

12.1 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.