Managed Access Agreement

Selpercatinib for treating advanced thyroid cancer with RET alterations [ID3744]

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Selpercatinib for treating advanced thyroid cancer with RET alterations [ID3744]

Company name: Eli Lilly and Company Limited

Primary source of data collection: Ongoing clinical study, LIBRETTO-001

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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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 selpercatinib for treating advanced thyroid cancer with RET alterations (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.

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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 2024

2.3 Eli Lilly and Company Limited 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 2024.

2.4 Eli Lilly and Company Limited 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 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.

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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 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 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:

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- 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 Eli Lilly and Company Limited 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 Eli Lilly and Company Limited do not make a submission to NICE for the purpose of updating the guidance, NICE and NHS England and NHS Improvement will require the company 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 NHS England and NHS Improvement, 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 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.

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- 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 selpercatinib in the Cancer Drugs Fund include:

- application is being made by and the first cycle of systemic anti-cancer therapy with selpercatinib will be prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy

- confirm that this patient is an adult with a proven histological or cytological diagnosis of non-medullary thyroid cancer or an adult or adolescent aged 12 years and older with a proven histological or cytological diagnosis of medullary thyroid cancer.

- confirm that this patient's thyroid cancer has been documented as having a RET fusion or RET mutation as determined by a validated genomic test.

- In the case of RET fusion positive non-medullary cancer confirm that either the patient has differentiated thyroid cancer (papillary/follicular/Hurtle cell) and has therefore been treated with lenvatinib or sorafenib or the patient has anaplastic thyroid cancer in which case no previous TKI treatment requirement is necessary. In the case of RET mutant medullary cancer confirm that the patient has been previously treated with cabozantinib or vandetanib.

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- confirm that the patient has an ECOG performance status (PS) of 0 or 1 or 2.
- confirm that selpercatinib is being given as monotherapy.
- confirm that the patient has not previously received selpercatinib or any other TKI which targets the RET receptor unless the patient has received selpercatinib via a company early access scheme and the patient meets all the other criteria listed here.
- confirm that selpercatinib is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment.
- confirm that I am aware of the following issues as regards the administration of selpercatinib as detailed in its Summary of Product Characteristics (SPC):
    - the dosage of selpercatinib is according to body weight
    - selpercatinib has reduced solubility at a higher pH and hence precautions are necessary with the co-administration of proton pump inhibitors or H2 antagonists
    - selpercatinib has clinically important interactions with CYP3A inhibitors or CYP3A inducers
- confirm that a formal medical review as to how selpercatinib is being tolerated and whether treatment with selpercatinib should continue or not will be scheduled to occur at least by the start of the third 4-weekly cycle of treatment.
- confirm that when a treatment break of more than 6 weeks beyond the expected 4-weekly cycle length is needed, I will complete a

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treatment break approval form to restart treatment, including indicating as appropriate if the patient had an extended break because of COVID-19.

- confirm that selpercatinib is to be otherwise used as set out in its Summary of Product Characteristics.

3.2 [redacted].

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

As estimated by the company	RET fusion positive thyroid cancer Year 1: [redacted] Year 2: [redacted] Year 3: [redacted] RET-mutant medullary thyroid cancer Year 1: [redacted] Year 2: [redacted] Year 3: [redacted]
As estimated by NICE Resource Impact Assessment team	RET fusion positive thyroid cancer Year 1: [redacted] Year 2: [redacted] Year 3: [redacted] RET-mutant medullary thyroid cancer Year 1: [redacted]

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	Year 2: [redacted] Year 3: [redacted]

Patient safety

3.4 The company have a responsibility to report any suspected unexpected serious adverse reactions (SUSARs). NICE and NHS England and NHS Improvement will assess any SUSARs and, if potential safety concerns are confirmed, will take steps, as appropriate, to mitigate the risk including but not limited to updating the eligibility criteria or recommending that the managed access be halted.

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 the progression-free and overall survival data in both the RET mutant medullary thyroid and RET fusion positive thyroid cancer populations,
2. Generalisability of data from the LIBRETTO-001 study to UK clinical practice in terms of prior treatment

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)	○ Phase 1/2 trial: LIBRETTO-001
Secondary sources	○ Systemic Anti-Cancer Therapy (SACT) dataset ○ NHS England and NHS Improvement's Blueteq data

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Description of sources

5.1 LIBRETTO-001 (NCT03157128) is an ongoing multicentre, open-label, phase I/II study in patients with advanced solid tumours, with RET activation.

Patients ≥12 years old with locally advanced or metastatic solid tumours, including *RET* fusion-positive solid tumours (e.g., NSCLC, thyroid, pancreas, colorectal), *RET*-mutant MTC, and other tumours with RET activation (e.g., mutations in other tumour types or other evidence of RET activation) who progressed on or were intolerant to standard therapy, or no standard therapy exists, or in the opinion of the Investigator, were not candidates for or would be unlikely to tolerate or derive significant clinical benefit from standard therapy, or declined standard therapy, and an ECOG ≤2 or LPS ≥40%. The primary analysis set (PAS) and integrated analysis set (IAS) for the pre-treated MTC cohort, and previously treated RET-fusion TC analysis set are the populations of interest under this agreement.

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. 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). PHE, through the National Cancer Registration and Analysis Service, does have permission to process confidential patient information (without prior patient consent) afforded through Regulation 2 of The Health Service (Control of Patient Information) Regulations 2002.

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

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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 Progression free survival and overall survival are the outcomes of interest and are reported outcomes from the LIBRETTO-001 trial. The data available in [redacted] will provide further evidence of progression free survival and overall survival in the trial populations under consideration in the CDF.

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, performance status and prior treatments received
- Treatment duration
- Overall survival

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

- Number of applications to start treatment

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7 Data analysis plan

Clinical trials

7.1 LIBRETTO-001 updated thyroid cancer (RET-mutant MTC & RET fusion thyroid cancer) data is expected no later than [redacted] based on an interim data cut in [redacted]. The final analysis will occur [redacted] after last patient has enrolled. For RET-mutant MTC this will be [redacted] (data available [redacted]). For RET fusion thyroid cancer this is expected to be no later than [redacted] (data available [redacted]), although these dates could change since enrolment is still on-going.

Other data

7.2 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 all clinical trial data listed above, Eli Lilly and Company Limited will be the owner

8.2 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

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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.

8.3 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 Public Health England, have been established with NHS Trusts and NHS England and NHS Improvement.

8.4 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. 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). PHE, through the National Cancer Registration and Analysis Service, does have permission to process confidential patient information (without prior patient consent) afforded through Regulation 2 of The Health Service (Control of Patient Information) Regulations 2002.

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.

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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 the 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 Eli Lilly and Company Limited , shall also apply between the parties to this data collection arrangement in relation to the performance of their obligations under this data collection arrangement

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11 Equality considerations

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

☐ Yes ☒ No

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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.