Cancer Drugs Fund

Managed Access Agreement

Palbociclib in combination with fulvestrant for treating metastatic, hormone-receptor positive, HER2-negative breast cancer after endocrine therapy [TA619]

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Palbociclib with fulvestrant for treating hormone receptor-positive, HER2-negative, advanced breast cancer [TA619]

Company name: Pfizer Ltd

Primary source of data collection: Ongoing PALOMA-3 clinical study

Secondary source of data collection: Public Health England routine population-wide cancer data sets, including Systemic Anti-Cancer Therapy (SACT) dataset, and NHS England's Blueteq data

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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 palbociclib with fulvestrant for treating hormone receptor-positive, HER2-negative, advanced breast cancer [TA619]. 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	August 2021

2.3 Pfizer 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 August 2021.

2.4 Pfizer acknowledges their 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 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.

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, 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 any risks
- 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 If a primary source of data is delayed or no longer reports outcome data that could resolve the uncertainties identified by the technology appraisal committee, NICE and NHSE may consider the data collection agreement no longer valid, and withdraw the technology from the Cancer Drugs Fund.

3 Patient eligibility

3.1 Key patient eligibility criteria for the use of palbociclib in combination with fulvestrant in the Cancer Drugs Fund include:

- The application for palbociclib in combination with fulvestrant is made by and the first cycle of palbociclib plus fulvestrant will be prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy
- Patient has histologically or cytologically documented oestrogen receptor positive and HER-2 negative breast cancer
- Patient has metastatic breast cancer or locally advanced breast cancer which is not amenable to curative treatment
- Patient is male or is female and if female is either post-menopausal or if pre- or peri-menopausal has undergone ovarian ablation or suppression with LHRH agonist treatment
- Patient has an ECOG performance status of 0 or 1 or 2
- Patient has received previous endocrine therapy according to one of the three populations as set out below as these are the groups on which the NICE Technology Appraisal for palbociclib plus fulvestrant focused. Please record which population the patient falls into:

  - Patient has progressive disease whilst still receiving adjuvant or neoadjuvant endocrine therapy for early breast cancer with no subsequent endocrine therapy received following disease progression or,
  - Patient has progressive disease within 12 or less months of completing adjuvant endocrine therapy for early breast cancer with no subsequent endocrine therapy received following disease progression or,
  - Patient has progressive disease on 1st line endocrine therapy for advanced/metastatic breast cancer with no subsequent endocrine therapy received following disease progression.

- Patient has had no prior treatment with a CDK 4/6 inhibitor unless either abemaciclib (in combination with fulvestrant) or ribociclib (in combination with fulvestrant) has been stopped within 6 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression or palbociclib has been received as part of an early access scheme for the combination of palbociclib plus fulvestrant and the patient meets all the other criteria set out in this form.
- Patient has had no prior treatment with fulvestrant
- Patient has had no prior treatment with everolimus
- Palbociclib will only be given in combination with a fulvestrant
- Treatment will continue until there is progressive disease or excessive toxicity or until the patient chooses to discontinue treatment, whichever is the sooner

- Treatment breaks of up to 6 weeks are allowed, but solely to allow toxicities to settle

- Palbociclib and fulvestrant will be otherwise used as set out in their Summaries of Product Characteristics (SPC) including the need for ECGs to be performed prior to treatment, after 2 weeks of treatment and after 4 weeks of therapy

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

As estimated by the company	2020 – [redacted] 2021 – [redacted] 2022 – [redacted]
As estimated by NICE Resource Impact Assessment team	Year 1 – [redacted] Year 2 – [redacted] Year 3 - [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. results of the network meta-analysis
2. extrapolation of overall survival
3. time-to-treatment discontinuation
4. time on and details of subsequent therapies

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)	○ Final data-cut from the PALOMA-3 trial
Secondary sources	○ Systemic Anti-Cancer Therapy (SACT) dataset ○ NHS England's Blueteq data

Description of sources

5.1 PALOMA-3 is the pivotal study of palbociclib in combination with fulvestrant for treating advanced hormone-receptor positive, HER2-negative breast cancer. PALOMA-3 is an international, multicentre, 2:1 randomised, double-blind, placebo-controlled, parallel-group, Phase 3 clinical study. The study included women aged 18 years or older and of any menopausal status, with HR-positive, HER2-negative advanced breast cancer (aBC) not amenable to resection or radiation therapy with curative intent or metastatic breast cancer, whose disease progressed during or soon after completion of prior endocrine therapy received in the (neo)adjuvant or advanced setting.

Reported outcomes include progression-free survival (PFS), overall survival (OS), objective response (OR), clinical benefit response (CBR), duration of response (DR), adverse events (AEs), health-related quality of life (HRQoL) and time to treatment discontinuation (TTD).

5.2 NHS England's Blueteq database captures the Cancer Drugs Fund population. NHS England 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 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 following outcomes which will help to reduce the uncertainties identified by the NICE committee are planned to be collected in the ongoing PALMOA-3 study:

- Overall survival data
- Time-to-treatment discontinuation

Further follow-up from PALOMA-3 could provide more certainty on the overall survival benefit of palbociclib plus fulvestrant, reducing the uncertainty within the network meta-analysis and the extrapolation of overall survival.

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
- Treatment duration
- Overall survival
- Subsequent treatments, to cover:

- Whether people receive subsequent everolimus plus exemestane or exemestane monotherapy

Given the timeframe of the managed access period, real-world data collected through SACT will not be mature enough to provide meaningful information of the number and treatment duration of subsequent therapies. SACT data may be mature enough to provide meaningful information on whether people receive subsequent everolimus plus exemestane or exemestane monotherapy directly after receiving palbociclib plus fulvestrant. The committee were aware these data may not be captured when recommending palbociclib plus fulvestrant in the Cancer Drugs Fund.

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

- Number of applications to start treatment
- Baseline patient characteristics, including gender, age, performance status.

7 Data analysis plan

Clinical trials

7.1 The final analysis of PALOMA-3 is due to be performed after the final overall survival event and will follow the analysis plan outlined in the trial protocol (due approximately by April 2021).

From the clinical study report, the efficacy analyses could be conducted for subpopulations, for example, according to: previous chemotherapy status, menopausal status at study entry, or previous lines of therapy for metastatic disease.

7.2 [redacted].

7.3 The database lock will occur once the last overall survival event has occurred, which is expected in [redacted]. The data will be available for the development of a company submission in [redacted]

Other data

7.4 At the end of the data collection period Public Health England will provide a final report for NHS England which provide analyses based on NHS England'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, Pfizer Ltd 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 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.

8.4 Blueteq's Cancer Drugs Fund system data is owned by NHS England. NHS England is responsible for implementing Blueteq data collection and generally for the analysis of these data. NHS England, 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 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's Blueteq system. This report will be provided to NHS England and the company at the end of the managed access period. The final report will form part of NHS England'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, 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.

10 Data protection

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