Cancer Drugs Fund

Managed Access Agreement

Ribociclib in combination with fulvestrant for treating advanced hormone-receptor positive, HER2-negative breast cancer [TA593]

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Ribociclib in combination with fulvestrant for treating advanced hormone-receptor positive, HER2-negative breast cancer [TA593]

Company name: Novartis Pharmaceuticals UK Ltd

Primary source of data collection: MONALEESA-3

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

NICE Agreement Manager	Brad Groves
NHS England Agreement Manager	Peter Clark
Public Health England Agreement Manager	Jem Rashbass
Novartis Pharmaceuticals UK Ltd Ltd Agreement Manager	Deb Lancaster

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 ribociclib in combination with fulvestrant for treating advanced hormone-receptor positive, HER2-negative breast cancer [TA593]**.** 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. The data collection period is anticipated to conclude in December 2020 based on the pivotal MONALEESA 3 study. The

final patient in this study will be followed up until this time point. The process for exiting the Cancer Drugs Fund will begin at this point and the review of the NICE guidance will start. An interim analysis is anticipated to be available [redacted] which will be assessed at a data review meeting. The final and interim analyses are event driven, pre-specified to report after 263 and 351 overall survival (OS) events have been observed. The dates of these analyses stated above are based on the current death rates in the study but are currently estimated to be at the [redacted] respectively (see section 5.1). The company will update NICE and NHS England if these anticipated dates are likely to change. The process for exiting the Cancer Drugs Fund will begin at the date specified (December 2020), and the review of the NICE guidance will start.

2.2 As part of the managed access agreement, the technology will continue to be available through the Cancer Drugs Fund after the data collection period has ended and while the guidance is being reviewed. This assumes that the data collection period ends as planned and the review of guidance follows the standard timelines described in the addendum to NICE's methods and processes when appraising cancer technologies.

2.3 Any changes to the terms or duration of any part of the managed access agreement must be approved by NICE and NHS England as co-signatories to the agreement.

2.4 If data collection is anticipated to conclude earlier than the timelines stated in the managed access agreement, for example due to earlier than anticipated reporting of an ongoing clinical trial:

- Where capacity allows NICE will endeavour to reschedule the CDF 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 outcomes will no longer provide meaningful data).

2.5 If data collection from an ongoing clinical trial is anticipated to be delayed, please note:

- Resource/capacity issues will not be accepted as reasons for delaying the associated CDF guidance review.
- Unless a strong compelling rationale is provided, the CDF guidance review will proceed according to the original timelines outlined in the MAA.
- It may not be possible to amend the date of the final SACT or real-world data report, in which case it will be available before the Clinical Study report is completed.

3 Patient eligibility

3.1 Ribociclib with fulvestrant is recommended for use within the Cancer Drugs Fund as an option for treating hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer in people who have had previous endocrine therapy only if exemestane plus everolimus is the most appropriate alternative to a cyclin-dependent kinase 4 and 6 (CDK 4/6) inhibitor.

3.2 Key patient eligibility criteria for the use of ribociclib in the Cancer Drugs Fund include:

- The application for ribociclib in combination with fulvestrant is made by and the first cycle of ribociclib 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 ribociclib 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) 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 or ribociclib has been received as part of an early access scheme for the combination of ribociclib 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
- Ribociclib 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
- Ribociclib 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

3.3 Some patients are receiving ribociclib (provided by Novartis) in combination with fulvestrant under a commercial free of charge scheme. The eligibility conditions for the Scheme are as follows:

- postmenopausal women (≥18yrs) and is an NHS patient based in the UK; and has either:
    - untreated advanced HR+/HER2– breast cancer, that has progressed during or within 12 months of (neo)adjuvant endocrine therapy; or

  - advanced HR+/HER2– breast cancer that has progressed after at least one line of prior endocrine therapy for advanced breast cancer (excluding those patients who have previously received a CDK4/6i)

- patient is administered ribociclib in accordance with the patient's treatment schedule and consistent with the applicable section of the ribociclib Summary of Product Characteristics, such that, if the patient has previously received free-of-charge ribociclib, they are continuing to derive clinical benefit from the therapy.

3.4 Only those patients in the Novartis commercial free of charge scheme who fulfill all the criteria for use in the CDF will be allowed to transfer to CDF funding eg only those patients with advanced HR+/HER2- breast cancer who have progressed on **one** line of prior endocrine therapy with no subsequent endocrine therapy received following disease progression for advanced breast cancer will be eligible for CDF funding.

3.5 NICE's resource impact assessment estimates that 2,300 patients are eligible to receive treatment per annum. Novartis estimate that around [redacted] patients will be treated between June 2019 and December 2020 (accounting for uptake and market share).

3.6 The average treatment duration is estimated to be around [redacted]. The overall survival is currently unknown ahead of the survival analyses from the MONALEESA-3 study as described above but from the economic model mean overall survival is estimated to be [redacted](undiscounted).

4 Area(s) of clinical uncertainty

4.1 The Appraisal Committee identified the following areas of uncertainty that may be addressed by the collection of further data:

- overall survival data from the pivotal clinical trial (MONALEESA 3) are uncertain due to the relatively short term follow up
- extrapolation of progression-free survival in the economic model Is uncertain due to the relatively short term follow up available from the clinical trial and
- post-progression survival is uncertain due to the relatively short term follow up available from the clinical trial.

5 Source(s) of data collection

Clinical trial

5.1 The primary source of data collection will be derived from the ongoing, international, multicentre, phase III, randomised controlled study - MONALEESA 3. A final data-cut and clinical study report is anticipated to be available in [redacted] when 351 overall survival events have been observed. An interim data cut is anticipated to be available at the [redacted] when 263 OS events have been observed. Progression-free survival, with longer duration of follow-up, will be provided in these clinical study reports.

Other data

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

5.3 Public Health England identifies, collects, collates, quality-assures and analyses large population-level datasets for specific diseases and conditions, including cancer. These datasets include the Systemic Anti-cancer Therapy (SACT) dataset, which is a mandated dataset as part of the Health and Social Care Information Standards. Public Health England will use the routinely captured data collected during the period of the data

collection arrangement to provide analyses as defined in sections 6.3 and 7.3

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, overall survival and safety data will continue to be collected in the MONALEESA-3 trial and future overall survival event-driven analyses are pre-specified in the protocol; estimated timings for availability of these analyses are provided above (Section 4.4). The data from this trial will help resolve the clinical uncertainty surrounding overall survival of patients, post-progression survival and extrapolation of progression free survival.

Other data, including SACT

6.2 Outcome data will not be collected for the relevant comparators.

6.3 Data will be collected via Public Health England's routine population-wide datasets, including the SACT dataset. This collection will support data collected in the clinical trial. During the managed access agreement period, Public Health England will collect data to provide information on duration of therapy unless it is determined by the SACT Operational Group that no meaningful data will be captured in during the period of data collection.

7 Data analysis plan

Clinical trials

7.1 The next overall survival analysis is planned after approximately 263 deaths have been observed in the overall study population. If overall survival is not statistically significant at this stage in the full analysis set, the final survival analysis will take place after approximately 351 deaths have been observed in the overall study population. Subgroup analyses, including the population

described in TA593 (patients who have received prior endocrine therapy), will report overall survival and progression free survival.

7.2 During the data collection period, the interim overall survival analysis planned for when 261 OS events have been observed, will be reported. This is expected by the [redacted].

Other data

7.3 At the end of the data collection period Public Health England will provide a final report for NHS England based on routinely collected population-wide data, including that collected via SACT. The report will present depersonalised summary data, including the total number of patients starting treatment and treatment duration. The necessary controls will be put in place to ensure that patient confidentiality is not put at risk. The report will be shared with Novartis Pharmaceuticals UK Ltd in advance of the planned review of guidance.

7.4 Completeness of SACT dataset reporting will be shared with NHS England and Novartis Pharmaceuticals UK Ltd at regular intervals during the data collection period. Public Health England will provide summary results for time on treatment and survival to NHS England and the Novartis Pharmaceuticals UK Ltd on an annual basis, to check the continuing validity of the period of the data collection arrangement.

8 Ownership of the data

8.1 For all clinical trial data listed above, Novartis Pharmaceuticals UK 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 was facilitated by the Public Health England Office for Data Release. Novartis Pharmaceuticals UK Ltd will not have access to the Public Health England patient data, but will receive de-personalised summary data, with appropriate controls in place to cover this. Public Health England will provide a report to NHS England and the Novartis Pharmaceuticals UK Ltd at the end of the managed access period.

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 CDF system data is owned by NHS England. NHS England is responsible for implementing Blueteq data collection and generally for analysis of these data. NHS England, however, shares Blueteq data with Public Health England for CDF 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 Publication of the analysis results of data collected by Public Health England, including through SACT and the data from Blueteq's CDF system, will be planned and implemented by Public Health England.

10 Data protection

10.1 The terms of clause 7 (data protection) of the managed access agreement, as apply between NHS England and Novartis Pharmaceuticals UK 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?

None identified

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.