

# **Cancer Drugs Fund**

## **Managed Access Agreement**

**Durvalumab for maintenance treatment of unresectable non-small cell lung cancer after platinum-based chemoradiation (ID1175)**

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Cancer Drugs Fund – Data Collection Arrangement

### Durvalumab for maintenance treatment of unresectable non-small cell lung cancer after platinum-based chemoradiation (ID1175)

**Company name:** AstraZeneca UK Ltd

**Primary source of data collection:** Ongoing clinical study, **PACIFIC**

**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 durvalumab for maintenance treatment of unresectable non-small cell lung cancer after platinum-based chemoradiation (ID1175). [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. The data collection period is anticipated to conclude in June 2021, with 5-year follow-up data from the PACIFIC clinical trial being available for re-submission in September 2021 (see section **Error! Reference source not found.** for further detail). The process for exiting the Cancer Drugs Fund will begin at this point 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:

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- 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 Durvalumab as monotherapy has been recommended for use within the Cancer Drugs Fund as an option for treating locally advanced, unresectable non-small cell lung cancer (NSCLC) in adults whose tumours express PD-L1 on  $\geq 1\%$  of tumour cells and whose disease has not progressed following **concurrent** platinum-based chemoradiation therapy.
- 3.2 Durvalumab was granted marketing authorisation by the European Commission on 24 September 2018 for the treatment of locally advanced, unresectable NSCLC in adults whose tumours express PD-L1 on  $\geq 1\%$  of tumour cells and whose disease has not progressed following platinum-based chemoradiation therapy.
- 3.3 Key patient eligibility criteria for the use of durvalumab in the Cancer Drugs Fund include:
- Application has been made by and the first cycle of systemic anti - cancer therapy with durvalumab 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

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adverse reactions due to anti-PD-L1 treatments including pneumonitis, colitis, nephritis, endocrinopathies and hepatitis.

- Patient has a histologically- or cytologically-confirmed diagnosis of non-small cell lung cancer.
- Patient has locally advanced and unresectable non-small cell lung cancer which is either stage IIIA or stage IIIB or stage IIIC.
- PD-L1 testing with an approved and validated test to determine the PD-L1 Tumour Proportion Score (TPS) has been done prior to this application and the result either demonstrates a PD-L1 score of  $\geq 1\%$  or the PD-L1 TPS cannot be ascertained despite an intent and a reasonable attempt to do so.
- Patient has completed treatment with 2 or more cycles (defined according to local practice) of platinum-based combination chemotherapy given concurrently with definitive radical radiotherapy.
  - Durvalumab is not approved by NICE for use after sequential chemotherapy and radiotherapy.
- Patient has been re-staged since chemoradiotherapy was completed and does not have any evidence of disease progression or metastatic spread.
- Patient will start his/her first treatment with durvalumab within 42 days of the last active treatment date of chemoradiotherapy.
- Patient has an ECOG performance status (PS) of 0 or 1.
- The maximum treatment duration with durvalumab will be 12 months, this being measured from the date of first durvalumab treatment.
  - The total active treatment period is a maximum of 12 months i.e. in those patients who have toxicity and thus have dose interruptions, the maximum number of treatment cycles is 26 2-weekly cycles.
- Treatment with durvalumab will continue until loss of clinical benefit or excessive toxicity or the patient decision to stop therapy or a treatment duration of 12 months has been completed, whichever is the sooner.

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- No re-treatment with durvalumab is allowed.
- Patient has not received prior treatment with an anti-PD-1, anti-PD-L1, anti-PD-L2, anti-CD137, or anti-Cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) antibody unless durvalumab has been received as part of AstraZeneca's early access program for durvalumab after concurrent chemoradiotherapy.
  - Patients treated in the AstraZeneca early access program with sequential chemotherapy and radiotherapy or any patient with PD-L1 TPS <1% or PD-L1 negative disease are not eligible for durvalumab from the CDF. For such patients who have already started durvalumab, AstraZeneca will continue to supply durvalumab as a consequence of its commitment in its early access program.
- A formal medical review as to whether treatment with durvalumab should continue or not will be scheduled to occur at least by the end of the first 6 weeks of treatment.
- Treatment breaks of up to 12 weeks beyond the expected 2-weekly cycle length are allowed but solely to allow any immune toxicities to settle.
- The licensed dose and frequency of durvalumab will be used.

3.4 Durvalumab was made available to UK patients through an Early Access Program (EAP) since September 2017. The program provides ethical access to durvalumab for patients, who in their treating physicians' opinion, had an unmet clinical need that could not be treated with approved and commercially available drugs. As of 11 March 2019, 189 patients in England have accessed durvalumab treatment through the EAP. Of these, 68 patients whose tumours express PD-L1 on  $\geq 1\%$  of tumour cells and who have received durvalumab after platinum-based concurrent chemoradiation therapy, are still on treatment (at the time of writing this document). Data from EAP patients will not be analysed by Public Health England as part of the data collection agreement.

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3.5 It is estimated by the Company that 289 patients in England will receive durvalumab for locally-advanced, unresected, Stage III NSCLC through the Cancer Drugs Fund during the managed access arrangement.

3.6 The maximum treatment duration is 12 months. The estimated average treatment duration within the Cancer Drugs Fund during the managed access arrangement period is [REDACTED], based on data from the PACIFIC study. Median overall survival (OS) for the durvalumab arm (PD-L1  $\geq$ 1% group) was not reached in the PACIFIC study. Based on data from landmark OS assessments in PACIFIC, it is estimated that ~75% of patients will be alive at 2 years from the start of durvalumab monotherapy.

#### 4 Area(s) of clinical uncertainty

4.1 The primary area of clinical uncertainty relates to the long-term progression-free survival (PFS) and overall survival (OS) benefit achieved with durvalumab after stopping treatment.

#### 5 Source(s) of data collection

##### ***PACIFIC clinical trial***

5.1 The primary source of data collection during the managed access arrangement period will be the ongoing **PACIFIC** study, a randomised, double-blind, placebo-controlled, international, Phase III clinical trial in patients with locally-advanced, unresectable, Stage III NSCLC whose disease has not progressed following two or more overlapping cycles of definitive, platinum-based CRT.

5.2 The PACIFIC study has met its primary endpoints of PFS and OS, demonstrating statistically-significant and clinically-meaningful benefit versus standard-of-care active follow-up (placebo). Patients in the study are being followed for survival to address regulatory requirements / post-marketing

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commitments. 5-year follow-up data from the study will be available in 2021. Additional data-cuts may be performed in the interim at the request of regulatory agencies.

### ***Other data***

- 5.3 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.
- 5.4 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.
- 5.5 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 outcome data that will be collected during the data collection arrangement is described below:
  - 5-year PFS and OS data from PACIFIC - This will provide an additional 3 years of follow-up relative to the evidence presented in the NICE appraisal 1175 (22 March 2018 data cut-off) and should resolve the clinical uncertainty regarding the longer-term survival benefit of durvalumab versus standard-of-care (active follow-up) in the patient population covered by this managed access arrangement.

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- In addition, data on subsequent therapies will also be collected. These data will be used to update the frequency, duration, and cost of subsequent therapies in the economic model.

### ***Other data, including SACT***

6.2 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 overall survival, 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 At the end of the data collection period, 5-year PFS and OS data from the PACIFIC study will be used to inform the long-term survival extrapolations in the cost-effectiveness model.
- 7.2 Any revisions in the timing of the 5-year data will be communicated with NICE. Regular update meetings will be set to track the progress of the data collection by Public Health England.

### ***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, overall survival 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 AstraZeneca in advance of the planned review of guidance.

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

## **8 Ownership of the data**

8.1 The data being collected from the PACIFIC study belongs to AstraZeneca. The data collection is being managed under the PACIFIC clinical trial protocol.

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. AstraZeneca 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 AstraZeneca 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

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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 AstraZeneca, 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

**12 Annex: List of supporting documents**

N/A

# **Commercial Access Agreement**

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**The contents of this document have been redacted as they are confidential**