Cancer Drugs Fund

Managed Access Agreement

Cemiplimab for treating cutaneous squamous cell carcinoma [ID1367]

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Cemiplimab for treating cutaneous squamous cell carcinoma [ID1367]

Company name: Sanofi

Primary source of data collection: Ongoing clinical study (EMPOWER-CSCC 1)

Secondary source of data collection: Retrospective chart review study and Systemic Anti-Cancer Therapy data set

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Sanofi Agreement Manager	Jessamy Baird, Director of Patient Access UK & Ireland

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 cemiplimab for treating cutaneous squamous cell carcinoma [ID1367] (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. The data collection period is anticipated to conclude in July 2021, when it is expected that long term follow-up data from the cemiplimab phase II clinical trial will become available based on a data

cut-off of [redacted] (see section 5.1). 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 The company is responsible for paying all associated charges for a Cancer Drugs Fund review. Further information is available on the NICE website

2.4 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.

2.5 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).

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

- NICE and NHS England should be informed immediately as co-signatories to the agreement
- Unless a strong compelling rationale is provided, the CDF guidance review will proceed according to the original timelines outlined in the MAA.

- Resource/capacity issues will not be accepted as reasons for delaying the associated CDF guidance review.
- 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 Cemiplimab as monotherapy is recommended for use in the Cancer Drugs Fund (CDF) for the treatment of adult patients with metastatic or locally advanced cutaneous squamous cell carcinoma who are not candidates for curative surgery or curative radiation. Cemiplimab will be stopped at 2 years of treatment, on disease progression or if there is unacceptable toxicity (whichever occurs first).

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

- patient has a histologically- or cytologically-confirmed diagnosis of cutaneous squamous cell carcinoma
- patient has either locally advanced disease or metastatic disease and is not a candidate for curative surgery or curative radiotherapy
- patient does not have a contra-indication to being treated with cemiplimab
    - immunocompromised patients were not included in the main cemiplimab clinical study. Cemiplimab should be used with caution in immunosuppressed patients and if cemiplimab is being administered to an immunocompromised patient, then a full evaluation and discussion with the patient of the benefits and the risks of treatment with cemiplimab (e.g. rejection of a solid organ transplant) must be undertaken

- cemiplimab is to be given solely as monotherapy
- treatment with cemiplimab will continue until loss of clinical benefit or unacceptable toxicity or withdrawal of patient consent or for a maximum treatment duration of 2 years (or 35 3-weekly cycles of cemiplimab), **whichever occurs first**
    - In those patients transferring from the Sanofi compassionate access scheme (see section 3.3), a maximum total treatment duration of 2 years of treatment applies
- patient is fit for treatment with cemiplimab **and** has an ECOG performance status score of 0 or 1
- patient has no symptomatically active brain metastases or leptomeningeal metastases
- 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 the patient has been entered into the Sanofi cemiplimab compassionate access scheme **and** all other treatment criteria are fulfilled (eg ECOG performance status)
- a formal medical review as to whether treatment with cemiplimab 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 cycle length are allowed but solely to allow any immune toxicities to settle

3.3 There is no Early Access to Medicines scheme in place for cemiplimab. Early access to cemiplimab on compassionate grounds was made available to eligible advanced CSCC patients in the UK via a named patient supply (NPS) scheme. Estimated final number of patients on this scheme in

England is 30. Data from these early access patients will not be included as part of the SACT data collection agreement. Patient receiving cemiplimab via the NPS who meet the CDF eligibility criteria for treatment with cemiplimab will be transferred to commercial stock within 90 days on marketing authorisation which will be funded by NHS England. NPS patients who do not meet the CDF eligibility for cemiplimab will continue to have their cemiplimab funded by Sanofi until treatment is discontinued as agreed by the treating healthcare professional.

3.4 The incidence of advanced CSCC is uncertain. The company estimates the maximum number of cemiplimab treated patients within the Cancer Drugs Fund during the managed access arrangement period to be between 84 to 226 annually. The NICE Resource Impact Assessment team estimate it to be between 229 and 411 annually.

3.5 The maximum treatment duration would be 2 years. The evidence for cemiplimab is currently immature therefore treatment duration and overall survival with cemiplimab is currently uncertain. Based on economic modelling, the mean duration of treatment with cemiplimab is expected to be around [redacted] months while the mean overall survival is estimated to be [redacted] years.

4 Area(s) of clinical uncertainty

4.1 The Appraisal Committee have noted the following key sources of clinical uncertainty:

- The baseline characteristics of patients included in the model
- Long-term treatment benefit of cemiplimab. In particular, the magnitude of any continued treatment benefit after a stopping rule
- Lack of reliable comparative evidence that is generalisable to UK clinical practice

5 Source(s) of data collection

Clinical trial

5.1 The primary source of data collection during the managed access agreement period will be the phase II cemiplimab clinical trial. The phase II clinical trial is a non-randomised, three-group, multicentre study evaluating the efficacy and safety of cemiplimab in patients with advanced CSCC, defined as patients with mCSCC or laCSCC who are not candidates for surgery or radiotherapy. Long term OS and PFS data from the phase II cemiplimab trial will become available from a data cut-off in [redacted] and this data is expected to be fully incorporated in the indirect treatment comparisons and the cemiplimab economic model by [redacted]. Table 1 provides a brief description of the trial.

Table 1 Trial Description

Study Name	**Phase II EMPOWER-CSCC 1**
Location	31 sites in the US, Australia and Germany.
Trial design	Non-randomised, three-group, multicentre, multinational Phase II study.
Primary outcome	ORR, assessed by independent central review, as per RECIST v1.1.
Other outcomes	• ORR based on investigator review, as per RECIST v1.1. • DoR, measured from the time of CR or PR (whichever was first recorded) until the first data of PD (radiographic), or mortality due to any cause. • TTR, determined by independent central review and by investigator assessment. • PFS, measured from the start of treatment until the first date of PD (radiographic) or mortality due to any cause. • OS, measured from the start of treatment until death due to any cause. • Safety, including AEs, irAEs and SAEs.
Key: AE, adverse event; CR, complete response; DoR, duration of response; irAE, immune-related adverse events; ORR, overall response rate; OS, overall survival; PD, progressive disease; PFS, progression-free survival; PR, partial response; RECIST, Response Evaluation Criteria In Solid Tumours; SAE, serious adverse events; TTR, time to response	

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.

5.5 Data from 106 advanced CSCC patients receiving the current standard of care in the UK, collected as part of the ongoing retrospective chart review study conducted by Sanofi, is expected to become available in [redacted]. This data is subsequently expected to be incorporated in the indirect treatment comparisons and the economic model in [redacted]. In addition, data from the retrospective chart review study from other European countries and the US is anticipated to be available in [redacted] with data being fully incorporated in the economic model in [redacted]. This study will provide data on OS and PFS alongside patient characteristics.

6 Outcome data

Clinical trial

6.1 As specified above, mature OS and PFS will become available from the cemiplimab phase II clinical trial based on a data cut-off of [redacted] This

significantly longer term follow-up data will be used to increase the certainty around the long term survival predictions for cemiplimab and in particular will provide evidence on the continued treatment benefit associated with cemiplimab beyond 2 years.

Other data, including SACT

6.2 Outcome data (OS and PFS alongside patient characteristics) from patients receiving the current standard of care, collected as part of the ongoing retrospective chart review study in the UK, is expected to become available in [redacted] and will be fully incorporated in the economic model in [redacted]. Data from the retrospective chart review study from other European countries and the US is anticipated to be available in [redacted] and will be fully incorporated in the economic model in [redacted]. This data will enable the creation of a UK-specific historical control arm of the current standard of care. The availability of patient-level data from this study alongside long term patient-level data from the phase II cemiplimab trial will allow more robust population-adjusted indirect comparisons, by allowing adjustment for more prognostic factors, to calculate the relative treatment effect of the progression-free and the overall survivals.

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 overall survival, duration of therapy and information on the baseline characteristics of UK patients receiving cemiplimab (obtained via Blueteq) unless it is determined by the SACT Operational Group that no meaningful data will be captured in during the period of data collection. The classification of patients disease as being metastatic (nodal or distant metastasis) or locally advanced will be obtained via Blueteq.

7 Data analysis plan

Clinical trials

7.1 At the end of the data collection period in July 2021, long term cemiplimab data on OS and PFS will become available. This analysis will follow the analysis plan outlined in the phase II trial protocol for OS and PFS. The time frame for the data collection was defined such that it will provide sufficient length of follow up to alleviate key uncertainties particularly around the continued treatment benefit associated with cemiplimab. To this end, the [redacted] data cut is anticipated to provide a significantly longer additional follow up of up to [redacted] months compared to the last data cut provided to NICE as part of the technical engagement process.

7.2 Interim analyses are not currently planned. However, if this is to occur at a later stage, details of these analyses will be communicated with NICE.

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 Sanofi in advance of the planned review of guidance.

7.4 Completeness of SACT dataset reporting will be shared with NHS England and Sanofi at regular intervals during the data collection period.

7.5 OS and PFS alongside baseline characteristics from patients receiving the current standard of care will become available from the retrospective chart review study as per the timeframe described previously. Availability of the individual patient-level data (IPD) from the retrospective chart review study alongside IPD from the cemiplimab trial will allow for more prognostic factors

to be adjusted for and thus will enable a more meaningful comparison using indirect treatment comparison (ITC) methodologies. Adjustment of more prognostic factors will reduce the between-study differences and will provide a more robust estimate of the relative treatment effect reducing the uncertainty associated with the current ITC analyses.

8 Ownership of the data

8.1 For all clinical trial data listed above as well as data from the retrospective chart review study, the manufacturer will be the owner

8.2 Governance arrangements for the ongoing clinical trial as well as the retrospective chart review study are in place in line with the standard approvals and ethical procedures followed as per the defined study protocols.

8.3 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. Sanofi 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 Sanofi at the end of the managed access period.

8.4 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.

8.5 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. Publication of the analysis from the retrospective chart review will be planned and implemented by Sanofi/Regeneron.

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 Sanofi, 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.