Managed Access Agreement

Amivantamab with carboplatin and pemetrexed for untreated EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer [TA1158]

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Cancer Drugs Fund – Data Collection Arrangement

Amivantamab with carboplatin and pemetrexed for untreated EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer [TA1158]

Company name: Johnson & Johnson Innovative Medicines UK (referred to hereafter as Johnson & Johnson)

Primary source of data collection: Ongoing clinical study (PAPILLON)

Secondary source of data collection: NHSE routine population-wide cancer data sets, including Systemic Anti-Cancer Therapy (SACT) data set

NICE Agreement Manager	[redacted]
NHSE Agreement Manager	[redacted]
NDRS (NHSE) Agreement Manager	[redacted]
Johnson & Johnson Agreement Manager	[redacted]

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 **Amivantamab with carboplatin and pemetrexed for untreated EGFR exon 20 insertion mutation-positive advanced non-small-cell lung cancer [TA1158]**. 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 a guidance update are:

End of data collection (primary source)	[redacted] This is the expected data cut-off (DCO) for final analysis (FA)
Data available for development of company submission	[redacted] This is the date that the overall survival (OS) data from FA will be available after data cleaning, expected 3 months after DCO
Anticipated company submission to NICE for a guidance update	[redacted] It is expected that it will take 6 months after data availability to develop a submission to NICE

a. This is a later date than the date specified in the managed access proposal [redacted]
b. This is an event driven trial and so the exact time point for when a sufficient number of death events have occurred in order to conduct final analysis is unknown

2.3 Johnson & Johnson anticipates that the additional data collected during the Cancer Drugs Fund period will be incorporated into an evidence submission and submitted to NICE by [redacted]. Besides the data collected in the CDF, Johnson & Johnson expect that it will take 6 months after PAPILLON FA OS data availability (expected [redacted]) to develop a comprehensive and robust evidence submission to NICE. This timeframe accounts for the time needed to update the model, write the submission, and re-validate the extrapolation curves for both the intervention (amivantamab with chemotherapy) and the comparator arm, in light of the updated OS data from FA.

2.4 Johnson & Johnson 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 the guidance update into the technology appraisal work programme to align with the estimated dates for the end of data collection.

2.6 The NICE guidance update will follow the process and methods applicable to guidance updates that are in place at the time the invitation to participate in the guidance update is issued. These may be different from the process and methods applicable to guidance updates when this technology entered into the managed access agreement.

2.7 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 guidance update follows the standard timelines.

2.8 The company is responsible for paying all associated charges for a guidance update. Note that this includes the 'change fee' if the Company does not provide sufficient notice to NICE regarding changes to the evaluation timelines. Please refer to the NICE website and Charging Procedure for further information.

2.9 The company must inform NICE and NHS England (NHSE) in writing of any anticipated changes to the estimated dates for data collection at the earliest opportunity.

2.10 Any changes to the terms or duration of any part of the data collection arrangement must be approved by NICE and NHSE.

2.11 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:

2.12 Where capacity allows, NICE will explore options to reschedule the guidance update date to align with the earlier reporting timelines.

2.13 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).

2.14 If data collection is anticipated to conclude later than the estimated dates for data collection, the company should note:

2.15 The company must submit a written request to NICE and NHSE, with details of the extension requested, including an explanation of the factors contributing to the request.

2.16 It may be necessary for the company to mitigate the impact of any delay, and reduce any risks of further delays.

2.17 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 NHSE to provide data over the extended period.

2.18 Johnson & Johnson acknowledge their responsibility to provide an evidence submission for this technology to NICE under all circumstances following a period of managed access.

2.19 In the event that Johnson & Johnson do not make a submission to NICE for the purpose of updating the guidance, NICE and NHSE will require the company to 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 NHSE, 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.

2.20 NICE and NHSE 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.
- 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 amivantamab with carboplatin plus pemetrexed (amivantamab with chemotherapy) in the Cancer Drugs Fund include:

3.2 The prescribing clinician must confirm that the patient meets all the following criteria:

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

- The patient has a histologically or cytologically documented non-small cell lung adenocarcinoma (NSCLC) that has been shown to exhibit an epidermal growth factor (EGFR) exon 20 insertion mutation, OR

  There is documented agreement by the lung MDT that the radiological appearances are in keeping with recurrent/locally advanced/metastatic NSCLC AND there is an informative circulating free DNA test result confirming the presence of an EGFR exon 20 insertion mutation.

  The selected option of the two given here will be indicated in the Blueteq record.

- The patient has locally advanced or metastatic disease, and that for this disease indication, the patient has not received any previous systemic anti-cancer therapy.

- The patient has an ECOG performance status (PS) of 0 or 1.

- The patient will be treated with amivantamab in combination with pemetrexed and carboplatin for an initial 4 x 3-weekly cycles, followed by pemetrexed in combination with amivantamab until loss of clinical benefit, or excessive toxicity, or patient choice to discontinue treatment, whichever is the sooner. If a patient experiences severe toxicity specifically related to pemetrexed, amivantamab can be continued as a single agent.

- The patient will be treated with the intravenous formulation of amivantamab. (Note – the subcutaneous formulation is NOT currently licensed in the UK for this indication).

- Where a treatment break of more than 6 weeks beyond the expected 3-weekly cycle length is needed, a treatment break approval form will be completed to restart treatment, which MUST be approved before treatment is recommenced.

- Amivantamab will otherwise be used as set out in its Summary of Product Characteristics (SPC).

3.3 Amivantamab with chemotherapy in this indication (1L treatment for patients with EGFR Exon20 insertion mutation-positive advanced NSCLC) is associated with a named patient programme which was closed to new patients at the point of MHRA approval. As of 15 December 2025, there are two patients receiving amivantamab with chemotherapy on this programme. There was also a named patient programme for the use of amivantamab monotherapy after prior chemotherapy (2L indication) which, as of December 2025, consists of one patient since 2021.

3.4 As of December 2025, two people in England have received amivantamab with chemotherapy as a first-line treatment for EGFR Exon20 insertion mutation-positive NSCLC. These early access patients will be included as part of the SACT data collection agreement because they will provide relevant outcomes data, especially survival, for this indication. These data can directly help reduce the uncertainty associated with the long-term benefit of amivantamab with chemotherapy, which is the remaining uncertainty in this appraisal. Including these patients will maximise the sample size of patients included in the SACT data collection, which is an important consideration in this very rare disease.

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

As estimated by the company	Year 1 = [redacted] Year 2 = [redacted] Year 3 = [redacted] The numbers above reflect the total eligible patient population in years 2026, 2027, and 2028 that are estimated from the company's budget impact model (BIM) which was submitted to NICE. It has been assumed that 100% of eligible patients would receive amivantamab with chemotherapy in lieu of any targeted or efficacious therapies available in this indication.
As estimated by NICE Resource Impact Assessment team	Year 1 = 106 Year 2 = 108 Year 3 = 109

4 Patient safety

4.1 The company and NHSE have the responsibility to monitor the safety profile of the technology and must provide an overview of any new or updated safety concerns to NICE. If any new safety concerns are confirmed, NICE and NHSE will take steps, as appropriate, to mitigate the risk including but not limited to updating the eligibility criteria or recommending that the managed access agreement be suspended.

5 Area(s) of clinical uncertainty

5.1 The appraisal committee identified the following key areas of uncertainty during the course of the appraisal process, described in the Final Draft Guidance:

- The immaturity of the overall survival (OS) data from the PAPILLON trial
- The extrapolations of OS in the amivantamab-chemotherapy arm

5.2 The committee expect further data collection will allow for a new model to be presented when the guidance is updated.

5.3 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 Draft Guidance.

6 Sources of data collection

Primary and secondary sources of data collection

Primary source(s)	Phase III, registrational clinical trial (PAPILLON)
Secondary sources	Systemic Anti-Cancer Therapy (SACT) dataset NHSE's Blueteq data

Description of sources

6.1 PAPILLON:

The PAPILLON trial is a global Phase 3, randomised, open-label multicentre study that provides the main clinical evidence base for amivantamab with carboplatin and pemetrexed (amivantamab with chemotherapy) compared

with carboplatin and pemetrexed (chemotherapy) in patients with untreated EGFR Exon 20 insertion mutation-positive advanced NSCLC.

Efficacy and safety data from the primary analysis (03 May DCO) were used as the main basis for the evidence submission to NICE. Efficacy data were presented from the full analysis set, comprising 153 patients in the amivantamab with chemotherapy arm and 155 patients in the chemotherapy arm. The total median duration of follow-up across both treatment arms was 14.92 months. However, for OS, data from an additional DCO (31st October 2023) are also presented, with a total median follow-up across both treatment arms of 20.9 months.

6.2 NHSE Blueteq database:

NHSE's Blueteq database captures the Cancer Drugs Fund population. 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). NHSE, through the National Disease Registration Service (NDRS), does have statutory authority to process confidential patient information (without prior patient consent) afforded through the NDRS Directions 2021 issued to it by the Secretary of State for Health and Social Care, and has issued the NDRS Data Provision Notice under section 259 of the Health and Social Care Act 2012 regarding collection of the Blueteq data from NHSE.

6.3 SACT database:

The Systemic Anti-Cancer Therapy (SACT) dataset, is a mandated dataset as part of the Health and Social Care Information Standards. NHSE is

responsible for the collection, collation, quality-assurance and analysis of this dataset.

6.4 NDRS in NHSE will collect data, including via the SACT dataset, alongside the primary source of data collection. The PAPILLON trial will be the primary source of data for an updated submission to NICE to secure a guidance update following the period of managed access.

7 Outcome data

Clinical trial

7.1 OS

Defined (as per protocol and statistical analysis plan) as the time from the date of randomization until the date of death due to any cause.

OS data from final analysis will address the unresolved uncertainties that have been highlighted by the committee in relation to this appraisal. The key uncertainty pertains to the long-term benefit associated with amivantamab with chemotherapy (also highlighted in section 6.1):

"*the effect of amivantamab with carboplatin and pemetrexed on how long people live is uncertain because there is limited clinical trial evidence" p3 Draft guidance*"

7.2 Other outcomes to be assessed at final analysis include: PFS (investigator assessed – primary endpoint), Overall response rate (ORR), duration of response (DOR), Time to subsequent therapy (TTST), Time to subsequent progression (TTSP), Time to second progression (PFS2), and safety data.

These outcomes will have a minor impact in resolving the unresolved clinical uncertainties raised by the NICE committee in relation to this appraisal, which is solely focused on the long-term survival benefit (i.e., OS).

Other data, including SACT

7.3 NDRS in NHSE 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 and performance status
- Treatment duration
- Overall survival

7.4 NHSE's Blueteq system will collect the following outcomes:

- Number of applications to start treatment

8 Data analysis plan

Clinical trials

8.1 The final analysis of OS will occur when approximately 210 deaths overall are anticipated (currently expected in [redacted]). The occurrence of death events drives for timeframe for when FA will occur. As this is an event-driven trial, the exact date of FA is therefore unknown.

OS will be analysed as per the statistical analysis plan, outlined in the trial protocol and summarised in the company's evidence submission.

OS will be analysed for the full population and for all pre-specified subgroups (ECOG performance status 0 or 1, and history of brain metastases yes or no). The final analysis will be conducted at a 2-sided alpha of 0.0498.

For OS, the treatment effect of amivantamab with chemotherapy arm will be compared with the chemotherapy arm based on a log-rank test stratified by ECOG performance status (0 or 1) and history of brain metastases (yes or no), using the Breslow approach for handling ties. The p-value generated from the stratified log-rank test will be used for hypothesis testing. The HR and the corresponding 95% CI will be estimated based on a stratified Cox's regression model, using the same stratification factors as for the log-rank test, with treatment as the sole explanatory variable.

8.2 There will be no updates or interim analyses during the period of managed access. The final analysis of the PAPILLON trial is the only update that will occur during the data collection period.

8.3 As per the timings given in section 2: the DCO for this FA is expected in [redacted].

The OS data from FA are expected to be available, after data cleaning, for inclusion into an evidence submission in [redacted].

Once the updated OS data are available, it is expected that it will take 6 months to develop an evidence submission to NICE which incorporates these data. This incorporates time to update the economic model, write the evidence submission, and re-validate the OS extrapolation curves with clinical experts in light of the updated OS data. Therefore, an evidence submission to NICE to secure a guidance update is expected in [redacted].

Other data

8.4 At the end of the data collection period NHSE will provide a final report which provide analyses based on NHSE'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 guidance update. 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.

9 Ownership of the data

9.1 For all clinical trial data listed above, Johnson & Johnson will be the owner.

9.2 This work uses data that has been provided by patients and collected by the NHS as part of their care and support. The data are collated, maintained and quality assured by the National Disease Registration Service, which is part of NHSE. The company will not have access to the NHSE patient data, but will receive de-personalised summary data, with appropriate governance controls in place.

9.3 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 NHSE, have been established with NHS Trusts and NHSE.

9.4 Blueteq's Cancer Drugs Fund system data is owned by NHSE. NHSE is responsible for implementing Blueteq data collection and generally for the analysis of these data. The lawfulness of this processing is covered under article 6(1)e of the United Kingdom General Data Protection Regulations (UK 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). NHSE, through the National Disease Registration Service, does have statutory authority to process confidential patient information (without prior patient consent) afforded through the National Disease Registries (NDRS) Directions 2021 issued to it by the Secretary of State for Health and Social Care. The lawfulness of NHSE's processing is covered under article 6(1)(c) of the UK GDPR – processing is necessary for compliance with a legal obligation to which the controller is subject (the NDRS Directions).

10 Publication

10.1 The details/authorship of any proposed publications arising from these studies will be planned with the publication of the final study results.

10.2 NDRS will produce a final report which includes analysis of data collected through SACT and from NHSE's Blueteq system. This report will be provided to NHSE and the company at the end of the managed access period. The final report will form part of NHSE's submission to the guidance update, and will therefore be publicly available at the conclusion of the guidance update.

10.3 NDRS will produce interim reports, which will be shared with 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 update.

10.4 Publication of any analyses and results from the NDRS reports undertaken as part of this DCA is not permitted until after the date of publication of the NICE committee papers (on the NICE website) following the first NICE guidance update committee meeting. Note manuscripts may be prepared using NDRS data before publication of NICE committee papers by prior agreement but publication is embargoed until after NICE publishes the data.

10.5 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.

11 Data protection

11.1 The terms of clause 7 (data protection) of the managed access agreement, that apply between NHSE and Johnson & Johnson, shall also apply between the parties to this data collection arrangement in relation to the performance of their obligations under this data collection arrangement

12 Equality considerations

12.1 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.