Managed Access Agreement

Pembrolizumab in combination with platinum-based chemotherapy for treating persistent, recurrent or metastatic cervical cancer [ID3798]

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Pembrolizumab in combination with platinum-based chemotherapy for treating persistent, recurrent or metastatic cervical cancer [ID3798]

Company name: Merck Sharp & Dohme (UK) Limited

Primary source of data collection: KEYNOTE-826

NICE Agreement Manager	Thomas Strong, Associate Director, Managed Access
NHSE Agreement Manager	Prof Peter Clark, CDF Clinical Lead
MSD Agreement Manager	Claire Grant, Head of HTA & OR, MSD

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 pembrolizumab in combination with platinum-based chemotherapy for treating persistent, recurrent or metastatic cervical cancer (ID3798) (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.

2.2 Estimated dates for data collection, reporting and submission are:

End of data collection (primary source)	[redacted]
Data available for development of company submission	N/A
Anticipated company submission to NICE	May 2023

2.3 MSD anticipate 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 May 2023.

2.4 MSD 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 exit from managed access 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 exit managed access using the NICE rapid review process. Further details on the rapid review process are available in the NICE manual.

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.

2.8 The company is responsible for paying all associated charges for a rapid review. Further information is available on the NICE website.

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 later than the estimated dates for data collection, the company should note:

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

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

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

2.14 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 pembrolizumab in the Cancer Drugs Fund include:

- the patient has a histologically- or cytologically-confirmed diagnosis of cervical carcinoma of:
    - squamous carcinoma
    - adeno-squamous carcinoma
    - adenocarcinoma
- the patient's tumour has been tested by an approved and validated test for PD-L1 expression as measured by the combined positive score (CPS) test and the result is 1 or more.
- The patient's current disease status is one of the following:
    - persistent locoregional disease with or without distant metastases

  - recurrent locoregional disease with or without distant metastases
  - first presentation with distant metastatic spread

- the patient's disease is currently not amenable to curative treatment (such as with surgery or radiotherapy or chemoradiotherapy)
- the types of treatment previously received by this patient for the cervical cancer are one of the following:
  - chemotherapy and surgery
  - radiotherapy and surgery
  - chemotherapy only
  - radiotherapy only
  - surgery only
  - none
- the patient has **either** not been previously treated with any systemic chemotherapy **or** has only received chemotherapy specifically used as a radio-sensitising agent
- the cytotoxic chemotherapy partner with the pembrolizumab is a combination chemotherapy with either paclitaxel plus cisplatin or paclitaxel plus carboplatin (AUC 5mg/mL/min)
  - Note: a maximum of 6 cycles of cytotoxic chemotherapy is to be administered

- bevacizumab is also to be given in combination with chemotherapy and pembrolizumab
    - Bevacizumab can be continued in combination with pembrolizumab beyond completion of chemotherapy if the patient is benefiting from treatment

- the patient will be treated with a fixed dose of pembrolizumab of either 200mg every 3 weeks or 400mg every 6 weeks.

- that treatment with pembrolizumab will be stopped at whichever of the following events occurs first: disease progression or unacceptable toxicity or withdrawal of patient consent or after 2 years of treatment (or after 35 x 3-weekly cycles or its equivalent if 6-weekly pembrolizumab is used).

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

- the patient has no symptomatically active brain metastases or leptomeningeal metastases

- a formal medical review as to how pembrolizumab and chemotherapy with or without bevacizumab are being tolerated and whether treatment with this combination should continue or not will be scheduled to occur at least by the end of the first 6 weeks of treatment

- where a treatment break of more than 12 weeks beyond the expected 3 or 6 weekly cycle length is needed, a treatment break approval form to restart treatment is to be completed, including indicating as appropriate if the patient had an extended break because of COVID 19.

- pembrolizumab, paclitaxel, cisplatin/carboplatin and bevacizumab will be otherwise used as set out in their respective Summary of Product Characteristics (SPCs).

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

As estimated by the company	First 12 months [redacted]
As estimated by NICE Resource Impact Assessment team	First 12 months 142

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:

1. The longer term overall survival estimates in the economic model were highly uncertain

2. The longer term progression-free survival and time to progression estimates are uncertain

6 Sources of data collection

Primary and secondary sources of data collection

Primary source(s)	○ KEYNOTE-826
Secondary sources	○ N/A

Description of sources

6.1 KEYNOTE-826 is a phase 3 randomized, double-blind, placebo-controlled trial of pembrolizumab plus chemotherapy versus chemotherapy plus placebo for the first-line treatment of persistent, recurrent, or metastatic cervical cancer. Primary endpoints are progression free survival (PFS) and overall survival (OS).

7 Outcome data

Clinical trial

7.1 Overall survival, progression-free survival, and time to progression data from the final analysis will be provided to address the committee's key clinical uncertainties.

7.2 Data analysis plan: The company will provide data from the Final Analysis of the KEYNOTE-826 clinical trial comprising of approximately 18 additional months of follow up. This will include updated survival analysis including OS, PFS and Time To Progression (TTP) and all other analyses necessary to update the existing economic model. An accompanying technical report will also be provided.

7.3 [redacted]

8 Ownership of the data

8.1 For all clinical trial data listed above, MSD will be the owner.

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.

10 Data protection

10.1 The terms of clause 7 (data protection) of the managed access agreement, that apply between NHSE and MSD, 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.