Cancer Drugs Fund

Managed Access Agreement

Pembrolizumab for treating relapsed or refractory classical Hodgkin lymphoma

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Pembrolizumab for treating patients with relapsed or refractory classical Hodgkin lymphoma [TA540]

Company name: Merck Sharp & Dohme Ltd.

Primary source of data collection: Public Health England routine population-wide cancer data sets, including Systemic Anti-Cancer Therapy data set and Hospital Episode Statistics

Secondary source of data collection: Clinical trial (KEYNOTE-087) and Bone marrow (stem cell) transplant register

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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 Pembrolizumab for treating patients with relapsed or refractory classical Hodgkin lymphoma, who are transplant ineligible and have failed treatment with brentuximab vedotin [TA540]. A positive recommendation within the context of a managed access agreement has been decided by the appraisal committee for a sub-population included within the appraised pembrolizumab classical Hodgkin lymphoma marketing authorisation.

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 July 2022. 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.

3 Patient eligibility

3.1 Pembrolizumab has been recommended for use in the Cancer Drugs for treating adults with relapsed or refractory classical Hodgkin lymphoma, who are transplant ineligible and have failed treatment with brentuximab vedotin. Note that this represents a subset of the marketing authorisation.

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

- The patient is an adult and has histologically documented classical Hodgkin lymphoma
- The patient has failed at least 2 lines of chemotherapy and also treatment with brentuximab vedotin
- The patient has not received stem cell transplantation of any kind
- The patient is currently ineligible for stem cell transplantation

- The patient is either a candidate for future stem cell transplantation if there is sufficient benefit of treatment with pembrolizumab or is not a candidate for stem cell transplantation however good the response to pembrolizumab may be
- The patient has an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 or 1
- The 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
- Pembrolizumab is being given as monotherapy and will commence at a fixed dose of 200 mg per infusion
- A formal medical review as to whether treatment with pembrolizumab should continue or not will be scheduled to occur at least by the end of the third cycle of treatment
- The patient will be treated until stem cell transplantation occurs or loss of clinical benefit or excessive toxicity or patient choice to discontinue treatment, whichever is the sooner
- The patient will receive a maximum treatment duration with pembrolizumab of 2 years
- Treatment breaks of up to 12 weeks beyond the expected cycle length are allowed but solely to allow immune toxicities to settle
- Pembrolizumab will otherwise be used as set out in its Summary of Product Characteristics (SPC)

3.3 There are no patients receiving pembrolizumab for this indication via means of a compassionate use or access program.

3.4 A maximum of 67 patients are estimated to receive treatment per annum.

3.5 The expected mean duration of treatment, based on patients who received a stem cell transplant from the KEYNOTE-087 trial, is [redacted]. As per the KEYNOTE-087 trial protocol, the maximum treatment duration would be 2 years. Median overall survival had not been reached at the time of the company's submission. However, using the two economic models considered by the NICE committee, a median survival of 63.06 months was estimated for the population relevant to this agreement.

4 Areas of clinical uncertainty

4.1 KEYNOTE-087, a non-comparative clinical trial, was designed to assess the use of pembrolizumab within the population described in this document. The committee reflected that the use of pembrolizumab as a bridge to allogeneic stem cell transplant reflected current clinical practice within England. However, KEYNOTE-087 was not designed as a bridge to transplant study; therefore, the following areas of uncertainty were identified by the committee:

- The time at which allogeneic stem cell transplant occurs.
- The proportion of patients who receive an allogeneic stem cell transplant

4.2 In addition the committee noted that the estimate of overall survival was uncertain. Due to inconsistencies between clinical practice and the KEYNOTE-087 trial design, the committee decided that estimates of overall survival could be sourced from the literature.

5 Sources of data collection

Public Health England routine population-wide cancer data sets and Hospital Episode Statistics

5.1 Public Health England routine population-wide data sets, including Systemic Anti-Cancer Therapy data set and 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.

5.2 Public Health England identifies, collects, collates, quality-assures and analyses large population-level data sets for specific diseases and conditions, including cancer. These data sets include the Systemic Anti-cancer Therapy (SACT) data set, which is a mandated data set 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 6.1 to 6.3 and 7.1 to 7.4.

5.3 Hospital Episode Statistics (HES) is a database containing details of all admissions, inpatient and outpatient appointments at NHS hospitals in England. Data is collected during a patient's time at hospital as part of the Commissioning Data Set and includes information relating to payment for activity undertaken. Public Health England holds an extract of identifiable HES data provided by NHS Digital. The use of identifiable HES data is only permitted where there is an appropriate legal basis.

5.4 Data sets collected and collated by Public Health England will be the primary sources of data collection.

Bone marrow (stem cell) transplant register

5.5 The UK bone marrow transplant registry is held at Guy's and St Thomas' and collects data on all bone marrow transplant in the UK. Public Health

England is exploring the possibility of gaining access to this data set. This could be used as a source of validation for the primary data sources. Public Health England will update NICE and the company on any progress relating to accessing this data source.

Clinical trial: KEYNOTE-087

5.6 KEYNOTE-087 is an ongoing phase II, multi-centre, single-arm, multi-cohort, non-randomised clinical trial. Cohort 2 of KEYNOTE-087 continues to be followed for survival outcome data. It is due to complete data collection in [redacted].

6 Outcome data

Systemic Anti-cancer Therapy data set

6.1 Data will be collected via Public Health England's routine population-wide data sets, including the SACT data set. During the managed access agreement period, Public Health England will collect data to provide information on overall survival and duration of therapy. Public Heath England are exploring SACT's collection of the specific regimens BEAM (carmustine, etoposide, cytarabine, melphalan), LEAM (as above but lomustine etoposide, cytarabine, melphalan) and Benda-EAM (bendamustine, etoposide, cytarabine, melphalan). These regimens are given as an adjuvant to a stem cell transplant. This should provide information on the proportion of patients who receive a stem cell transplant, the time from commencing treatment to transplant and intention to transplant (obtained via Blueteq).

Hospital Episode Statistics

6.2 Inpatient data will be collected by NHS Digital; Public Health England will seek to gain access to this data. Public Health England will collate data on the proportion of patients who receive a stem cell transplant and the date of transplant.

Bone marrow (stem cell) transplant register

6.3 The database can provide the proportion of patients who receive a stem cell transplant and the time of the transplant. However, it is anticipated that there may be difficulties in linking these data to other national data sets. This would mean that it may not be possible to identify those patients that have received pembrolizumab and the timing of the treatment. While these data sources will be explored further, it is anticipated that it may not be able to provide the outcomes required to resolve the clinical uncertainty.

Clinical trial: KEYNOTE-087

6.4 KEYNOTE-087 may provide bone marrow transplant data however it may not fully reflect UK clinical practice. It is expected that data can be obtained relating to OS for patients irrespective of stem cell transplant. These data can be used to support the UK specific data from SACT. However given differences between UK clinical practice and the trial design, there may be limited value in comparing these data sources.

7 Data analysis plan

Public Health England routine population-wide cancer data sets and Hospital Episode Statistics

7.1 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 the SACT database. The report will present depersonalised summary data, including the total number of patients starting treatment, overall survival, treatment duration, the proportion of people who go on to a stem cell transplant and time to transplant (weeks). The necessary controls will be put in place to ensure that patient confidentiality is not put at risk. The report will be shared with MSD UK Ltd in advance of the planned review of guidance.

7.2 Completeness of SACT data set reporting will be shared with NHS England and the MSD UK Ltd on a quarterly basis. Public Health England will provide summary results for time on treatment and survival to NHS England and the MSD UK Ltd on an annual basis, to check the continuing validity of the period of the data collection arrangement.

Bone marrow (stem cell) transplant register

7.3 Public Health England will update NICE and NHS England on any progress with the bone marrow transplant registry at quarterly meeting. Any analytical and reporting requirements will be discussed if access to the data set is possible.

Clinical trial: KEYNOTE-087

7.4 MSD expects a final updated survival report for KEYNOTE-087 based on a [redacted]. Data relevant to the population described in this DCA will be explored. Data of relevance will represent two subsets of the overall study population (n=81). Data will be described according to those patients who received a stem cell transplant following treatment with pembrolizumab; and will also be reported separately for those patients who did not receive a stem cell transplant following treatment with pembrolizumab. These data may be used to support data collected from SACT.

7.5 There are no interim analyses planned for KEYNOTE-087; therefore survival follow-up data as described in Section 7.1 are relevant.

8 Ownership of the data

8.1 For all clinical trial data listed above, MSD 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. MSD 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 MSD UK Ltd at the end of the managed access period.

8.3 The SACT data set is a mandated data set as part of the Health and Social Care Information Standards. All necessary governance arrangements through SACT, and other data sets 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.

8.5 Hospital Episode Statistics are derived from patient-level information collected by NHS Digital. Permission for access and use of the data has been granted to 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, HES 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 MSD 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.

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.