Cancer Drugs Fund

Managed Access Agreement

Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma [TA573]

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma [TA573]

Company name: Janssen-Cilag Ltd

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

Secondary source of data collection: Public Health England routine population-wide cancer data sets, including Systemic Anti-Cancer Therapy data set

NICE Agreement Manager	Carla Deakin
NHS England Agreement Manager	Peter Clark
Public Health England Agreement Manager	Rebecca Smittenaar
Janssen-Cilag Ltd Agreement Manager	Jennifer Lee

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 daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma [TA573]. 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 January 2021 when the final overall survival analysis data from the ongoing CASTOR trial will be available. 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:

- 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.

2.6 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 Daratumumab plus bortezomib plus dexamethasone has been recommended for use within the Cancer Drugs Fund as an option for treating relapsed multiple myeloma in people who have had 1 previous treatment in line with the patient eligibility criteria listed in section 3.2 below.

3.2 Key patient eligibility criteria for the use of daratumumab with bortezomib in the Cancer Drugs Fund include:

- patient has a diagnosis of multiple myeloma
- patient has received **1 and no more than 1 prior line of treatment** and that the numbering of a line of treatment is in accordance with the International Myeloma Workshop Consensus recommendations for the uniform reporting of clinical trials.
    - a line of therapy is defined as one or more cycles of a planned treatment program. This may consist of one or more planned cycles of single-agent therapy or combination therapy, as well as a sequence of treatments administered in a planned manner (i.e. induction chemotherapy/chemotherapies when followed by stem cell transplantation is considered to be 1 line of therapy)
    - a new line of therapy starts when a planned course of therapy is modified to include other treatment agents (alone or in combination) as a result of disease progression, relapse or toxicity, the exception to this being the need to attain a sufficient response for stem cell transplantation to proceed.
    - a new line of therapy also starts when a planned period of observation off therapy is interrupted by a need for additional treatment for the disease.

- the patient responded to the 1-prior line of treatment
- the patient now has documented relapse of disease after initial response to the 1-prior line of systemic therapy
- the patient has **either** not been previously treated with bortezomib **or** has been previously treated with bortezomib in which case the patient must not have progressed during bortezomib therapy
- the patient is of ECOG performance status 0 or 1 or 2
- the patient has had no previous therapy with daratumumab or an anti-CD38 antibody
- daratumumab is only to be used in combination with bortezomib and dexamethasone and that it is **not** to be used in combination with any other agents
- the dosage schedule of daratumumab will be for weekly treatment given weeks 1-9 (a total of 9 doses), 3-weekly treatment in weeks 10 to 24 (a total of 5 doses) and 4-weekly treatment from week 25 onwards
- the dosage schedule of bortezomib will be for a maximum of 8 cycles
- daratumumab is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment
- a formal medical review as to whether treatment with daratumumab in combination with bortezomib and dexamethasone continues or not will be scheduled to occur at least by the end of the first 6 weeks of treatment

- no treatment breaks of more than 6 weeks beyond the expected cycle length are allowed (to allow any toxicity of current therapy to settle or intercurrent comorbidities to improve)

- daratumumab to be otherwise used as set out in its Summary of Product Characteristics

3.3 In 2015, 5,540 people were diagnosed with MM in England (Cancer Research UK) and an estimated 61% of patients received two lines of therapy in clinical practice (Yong, 2016). Of these patients, approximately 8% are expected to enter clinical trials over the period of the MAA. Therefore, 2,882 relapsed MM patients are expected to meet the above criteria per annum. In year 1 30% (865 patients per annum) are expected to be treated with daratumumab in combination with bortezomib and dexamethasone and 70% (2,017 patients per annum) in years thereafter.

3.4 Daratumumab is administered on a treat-to-progression basis. It is anticipated that median treatment duration (time on treatment per patient) within the CDF during the full MAA period will be 24 months, as observed in the CASTOR trial.

4 Area(s) of clinical uncertainty

4.1 The key area of uncertainty identified in this appraisal which could be addressed within the MAA data collection period is overall survival (OS) in daratumumab patients. Despite 4 years of follow up, median OS for daratumumab patients has not yet been reached in CASTOR. Current expectations, based on event rates observed in CASTOR, are that median OS will be reached by January 2021 (after 6 years).

5 Source(s) of data collection

Clinical trial

5.1 CASTOR is the pivotal phase III, multicentre, randomised, open-label, active-controlled study comparing daratumumab with bortezomib and dexamethasone with bortezomib and dexamethasone among patients with relapsed MM who had received at least one prior line of therapy.

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.

6 Outcome data

Clinical trial

6.1 OS data will continue to be collected from CASTOR until final analysis (after ~320 events, estimated January 2021), at which point it is expected that median OS will be reached for daratumumab. These data will be used to validate the extrapolation of OS used in the economic model.

Other data, including SACT

6.2 During the managed access agreement period, Public Health England will collect data to provide information on treatment duration and overall survival, 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 The final analysis will follow the analysis plan outlined in the trial protocol. At the final OS analysis (after ~320 events), a stratified OS analysis will be performed. Stratification factors that are used in the analyses include ISS staging (I, II, III), number of prior lines therapy (1 vs. 2 or 3 vs. >3), and prior bortezomib treatment (no vs. yes). At the final OS analysis, overall survival will be reported for the intention to treat population and the population of interest: those who have received one prior treatment only. Additionally, a forest plot of subgroup analyses on OS will be generated.

Other data

7.2 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, treatment duration and overall survival. The necessary controls will be put in place to ensure that patient confidentiality is not put at risk. The report will be shared with Janssen-Cilag Ltd in advance of the planned review of guidance.

7.3 Completeness of SACT dataset reporting will be shared with NHS England and Janssen-Cilag Ltd at regular intervals during the data collection period. Public Health England will provide summary results for survival to NHS England and Janssen-Cilag Ltd on an annual basis, to check the continuing validity of the period of the data collection arrangement.

8 Ownership of the data

8.1 For all clinical trial data listed above, Janssen-Cilag 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. Janssen-Cilag 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 Janssen-Cilag Ltd 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 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 Janssen-Cilag 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

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.