

# **Cancer Drugs Fund**

## **Managed Access Agreement**

**Ixazomib with lenalidomide and  
dexamethasone for treating relapsed or  
refractory multiple myeloma**

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Cancer Drugs Fund – Data Collection Arrangement

### Ixazomib citrate in combination with lenalidomide and dexamethasone for relapsed/refractory multiple myeloma

**Company name:** Takeda UK Limited.

**Primary source of data collection:** Ongoing Phase III TOURMALINE MM-1 study

**Secondary source of data collection:** Public Health England routine population-wide cancer data sets including Systemic Anti-Cancer Therapy (SACT) data set and the NHS England Blueteq CDF system.

**Supporting evidence:** Additional data from real world evidence in the UK Named Patient Programme may be submitted to support the aforementioned primary and secondary sources of data collection.

<b>NICE Agreement Manager</b>	Linda Landells, Associate Director
<b>NHS England Agreement Manager</b>	Prof Peter Clark, CDF Clinical Lead
<b>Public Health England Agreement Manager</b>	Martine Bomb, Head of Data Projects
<b>Takeda UK Ltd. Agreement Manager</b>	Emma Roffe, Head of Medical & Scientific Affairs – Oncology

## 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 ixazomib citrate in combination with lenalidomide and dexamethasone for relapsed or refractory multiple myeloma [ID807] (to be updated with TA number after final guidance has been published). A positive recommendation within the context of a managed access agreement 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 for the primary source of data is anticipated to conclude with the availability of a final overall

survival analysis of the TOURMALINE MM-1 trial which is currently expected in December 2019 (this final analysis is event driven so may be earlier or later than this date) (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.

### **3 Patient eligibility**

- 3.1 Ixazomib in combination with lenalidomide and dexamethasone has been recommended for use in the Cancer Drugs Fund for the treatment of adult patients with multiple myeloma who have received 2 or 3 prior lines of therapy.

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

- Confirmed diagnosis of multiple myeloma
- Patient has previously received 2 or 3 prior lines of treatment (induction chemotherapy and stem cell transplant is considered to be 1 line of therapy).  
Note: Patients previously treated with 1 or >3 lines of treatment are not eligible for ixazomib
- Patient must not be refractory to previous proteasome inhibitor-based or lenalidomide-based treatment at any line of therapy (in this context, refractory disease is defined as disease progression on treatment or disease progression within 60 days of the last dose of a proteasome inhibitor or lenalidomide).

Note: as lenalidomide is only commissioned by NHS England after

2 prior therapies, the only eligible patients who have had prior lenalidomide must have received it in the context of a clinical trial in an earlier line of therapy. Such patients must not be refractory to lenalidomide according to the above definition.

- The patient has either been refractory to 1 or more lines of therapy or has responded and relapsed after each line of therapy.
- Acknowledgement whether a patient has been treated with a previous autologous or allogenic stem cell transplant or not.
- The patient must be treatment-naïve to any therapy with ixazomib
- Ixazomib is only to be used in combination with lenalidomide and dexamethasone
- Ixazomib is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment, whichever is the sooner
- Performance status of the patients must be 0 or 1 or 2
- 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)
- Ixazomib to be otherwise used as set out in its Summary of Product Characteristics

3.3 It is estimated that between 400-800 patients annually (approximately 800-1600 over the entire agreement) will be treated with ixazomib within the Cancer Drugs Fund during the course of the managed access arrangement period. The estimated number of patients who will be treated with ixazomib within the Cancer Drugs Fund is an estimate based on currently available information but is uncertain and may change.

3.4 The average (mean) treatment duration for a patient within the TOURMALINE MM-1 trial was approximately 20 cycles. It is estimated that the treatment duration within the Cancer Drugs Fund during the managed access agreement period will be similar.

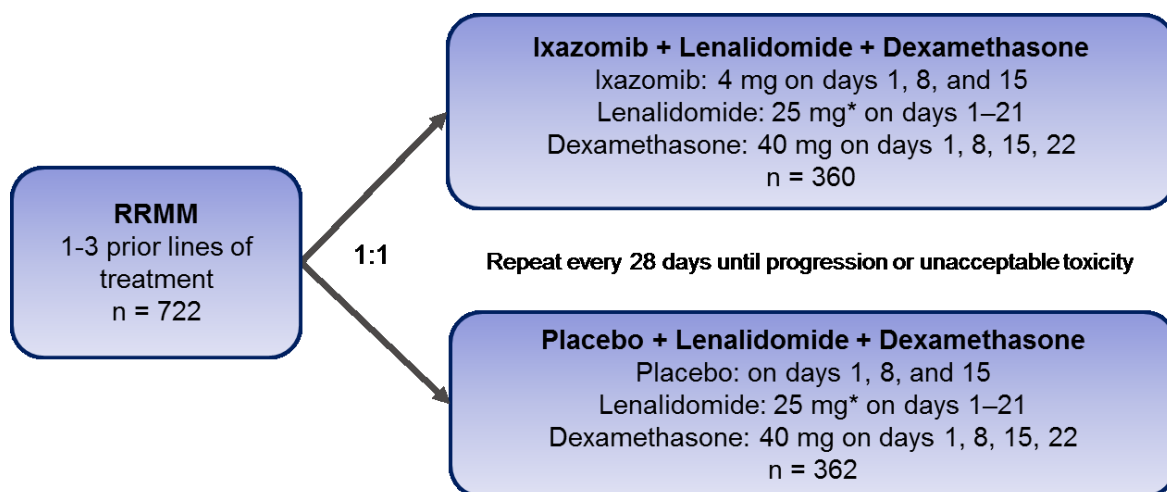
**4 Area(s) of clinical uncertainty**

- 4.1 Ixazomib has a conditional marketing authorisation based on data from the Phase III TOURMALINE MM-1 clinical trial. The committee noted that due to the immaturity of the data from this trial (follow-up remains ongoing), the key areas of uncertainty are the magnitude of the clinical benefit of ixazomib on overall survival (OS) and the duration of treatment with ixazomib. A secondary area of uncertainty is health related quality of life and therefore any further data on utilities from EQ 5D would be welcomed.

**5 Source(s) of data collection**

***TOURMALINE MM-1***

- 5.1 It is anticipated that the key areas of clinical uncertainty (the magnitude of the increase in OS, health related quality of life and duration of treatment) will be addressed with maturation of the ongoing Phase III TOURMALINE MM-1 trial. The final analysis of OS is event driven and is expected to report in December 2019. It is anticipated that a clinical study report will be available approximately 4 months following internal release of the data. Takeda will inform NICE and the Cancer Drugs Fund if there are any changes to the expected timeline on a regular basis. The TOURMALINE MM-1 trial will be the primary source of data to inform the appraisal submission following the conclusion of the data collection period through the Cancer Drugs Fund.
- 5.2 TOURMALINE MM-1 is a phase III, global, double-blind, randomised, placebo-controlled study. The study design is as follows:



- **Primary endpoint:** progression-free survival
- **Key secondary endpoints:** OS and OS in patients with del(17p)

**Other secondary endpoints included:** overall response rate, OS and progression-free survival in patients with high-risk cytogenetics, quality of life, adverse events.

### Other data (SACT)

5.3 NHS England’s Blueteq database captures the Cancer Drugs Fund population. NHS England shares Blueteq data with Public Health England for the Cancer Drugs Fund evaluation purposes. That sharing is governed by a data sharing agreement between NHS England and Public Health England.

5.4 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 estimates of:

- Duration of therapy
- Overall survival (secondary data source to the TOURMALINE MM-1 trial)

5.5 Data will be collected via SACT dataset and Blueteq alongside the primary source of data collection, TOURMALINE MM-1. During the managed access agreement period, PHE will collect data on duration of treatment and reason for discontinuation (including death, progression, acute chemotherapy toxicity and patient choice). In addition, PHE will collect data on underlying patient characteristics such as age, gender and race/ethnicity (if available). The Blueteq database will collect information on the number of prior lines of therapy (i.e. 2 or 3 prior lines).

***Other data (Real world evidence)***

5.6 In addition to data from the primary and secondary sources of data collection, any available data from the real world use of ixazomib (e.g. from the UK Named Patient Programme within the recommended population) may be used to support the submission following the Cancer Drugs Fund data collection period.

5.7 Patients in England who have received ixazomib via the Named Patient Programme could potentially form part of the Cancer Drugs Fund data collection population. The eligibility for the Named Patient Programme was as per the entry criteria for the TOURMALINE MM-1 trial. The key eligibility criteria included

- Adult patients with relapsed and/or refractory multiple myeloma
- Patient has received one to three prior lines of therapy
- Patient is not refractory to lenalidomide or a proteasome inhibitor

Only patients who correspond to the Cancer Drugs Fund recommended population will be considered for inclusion in the data collection from real world evidence sources.

**6 Outcome data**

***Clinical trial***

6.1 The key outcomes to be measured are overall survival and duration of treatment. Secondary outcomes of interest include updated utility data (via

EQ 5D). At the end of the data collection period, mature data will be available from the final analysis of TOURMALINE MM-1. This data will be the primary source of information used to update the health economic model.

### ***Other data, including SACT***

6.2 Data will be collected via Public Health England's routine population-wide datasets, including the SACT dataset. This collection will support data from TOURMALINE MM-1. During the data collection period, Public Health England will collect data to provide information on overall survival, treatment duration and line of therapy (obtained via Blueteq). Additional data on treatment duration may be provided from the UK Named Patient Programme.

## **7 Data analysis plan**

### ***Clinical trials***

7.1 At the end of the data collection period, the primary outcomes of overall survival and duration of treatment data from the final statistical analysis of TOURMALINE MM-1 will be used to inform the long-term extrapolation in the health economic model. Secondary outcomes that may also feed into the model include utilities from the EQ 5D.

7.2 Any revisions in the timing of the final analysis from TOURMALINE MM-1 will be communicated to NICE.

### ***Other data***

7.3 Public Health England will provide a number reports for NHS England, NICE and Takeda based on routinely collected population-wide data, including that collected via SACT/Blueteq, during the data collection period. The necessary controls will be put in place to ensure that patient confidentiality is not put at risk.

7.4 Completeness of relevant items from the routine population based datasets collated by Public Health England will be shared with Takeda on a quarterly basis. Additionally, Public Health England will provide a report for NHS England, NICE and Takeda on an annual basis, depersonalised summary



results for line of therapy, patient and tumour characteristics, treatment duration and reason for discontinuation to NHS England until the end of the data collection period. At the end of the data collection period, PHE will provide a final report of depersonalised summary data on the aforementioned outcomes. The report will be shared with Takeda prior to the review of the appraisal.

## **8 Ownership of the data**

- 8.1 For all clinical trial data listed above, Takeda 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. Takeda will not have access to Public Health England identifiable patient data, but will receive de-personalised data, with appropriate controls in place to cover this. Public Health England will provide a report to NHS England at the end of the managed access period, which will be shared with Takeda.
- 8.3 The SACT dataset is a mandated dataset as part of the Health and Social Care Information Standards. Identifiable individual patient data will remain within Public Health England premises and there will not be any data sharing of individual identifiable patient data outside of Public Health England. All necessary governance arrangements through SACT, and other datasets brought together by Public Health England, have been established with NHS Trusts.
- 8.4 Blueteq's CDF system data is owned by NHS England. NHS England is responsible for implementing Blueteq data collection and analysis. NHS England shares Blueteq data with Public Health England for Cancer Drug Fund evaluation purposes. That sharing is governed by a data sharing agreement between NHS England and Public Health England.

8.5 For real world evidence (not including data collated by PHE; including data from the Named Patient Programme) the data will be owned by the organisation responsible for collecting the data.

## **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 any data collected by Public Health England, including through SACT, alongside the primary data source will be planned by Public Health England. Takeda will be given access to the report produced for NHS England for the review of the appraisal before the planned start of the review.

9.3 Publication of the analysis results of Blueteq's CDF system data collected alongside the primary data source will be planned by NHS England. Takeda will be given access to the report produced for the review of the appraisal before the planned start of the review.

# **Commercial Access Agreement**

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**The contents of this document have been  
redacted as they are confidential**