# Cancer Drugs Fund

# Managed Access Agreement

## Brexucabtagene autoleucel for treating relapsed or refractory mantle cell lymphoma [TA677]

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Cancer Drugs Fund – Data Collection Arrangement

## Brexucabtagene autoleucel for treating relapsed or refractory mantle cell lymphoma [TA677]

**Company name:** Gilead Sciences Ltd (the legal entity in the UK for Kite, a Gilead company) and referred to as Kite in this Agreement

**Primary source of data collection**: Ongoing clinical trial (ZUMA-2 NCT02601313)

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

| | |
|---|---|
| **NICE Agreement Manager** | Brad Groves, Associate Director, Managed Access |
| **NHS England and NHS Improvement Agreement Manager** | Prof Peter Clark, CDF Clinical Lead |
| **Public Health England Agreement Manager** | Martine Bomb, Analytical Lead |
| **Kite Agreement Manager** | Eleonora Lovato |

### 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 brexucabtagene autoleucel for treating relapsed or refractory mantle cell lymphoma [TA677].
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 CDF guidance review are:

| | |
|---|---|
| **End of data collection (primary source)** | [redacted] |
| **Data available for development of company submission** | [redacted] |
| **Anticipated company submission to NICE for Cancer Drugs Fund review** | Estimated to be February 2025 |

2.3 Kite 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 February 2025.

2.4 Kite acknowledge their responsibility to adhere as closely as possible to the timelines presented in the document.

2.5 NICE will, as far as is practicable, schedule a Cancer Drugs Fund review into the technology appraisal work programme to align with the estimated dates for the end of data collection. The review will use the process and methods in place at the time the invitation to participate in the guidance review is issued, which will be no earlier than 4 weeks prior to the anticipated company submission date. For further details of the expected timelines for the Cancer Drugs Fund guidance review see 6.27 of the technology appraisal process guide.

2.6 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 review of guidance

follows the Cancer Drugs Fund guidance review timelines described in NICE's guide to the processes of technology appraisal.

2.7 Kite is responsible for paying all charges for the undertaking of a Cancer Drugs Fund review, which are detailed on the NICE website.

2.8 Kite must inform NICE and NHS England and NHS Improvement of any anticipated changes to the estimated dates for data collection at the earliest opportunity.

2.9 Any changes to the terms or duration of any part of the data collection arrangement must be approved by NICE and NHS England and NHS Improvement.

2.10 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, Kite should note:

- Where capacity allows, NICE will explore options to reschedule the Cancer Drugs Fund 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 outputs will no longer provide meaningful data).

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

- Kite must submit a written request to NICE and NHS England and NHS Improvement, 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.

- 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 Public Health England to provide data over the extended period.

2.12 NICE and NHS England and NHS Improvement 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 brexucabtagene autoleucel in the Cancer Drugs Fund include:

For leucapheresis and manufacture of CAR-T cells:

- application is made by leucapheresis and treatment with brexucabtagene autoleucel-modified CAR-T cells is initiated by a consultant haematologist or medical oncologist specifically trained and accredited in the use of systemic anti-cancer therapy and working in an accredited CAR-T cell treatment centre **and** who is a member of the National CAR-T Clinical Panel for MCL **and** a member of the treating Trust's MCL and CAR-T cell multidisciplinary teams.

- patient has a confirmed histological diagnosis of MCL with documentation of either cyclin D1 overexpression or the presence of

the translocation t(11:14) and this diagnosis has been confirmed by a designated lymphoma stem cell transplant centre.

- Patient has relapsed or refractory MCL defined by one of the following:
    - Refractory disease is defined as being either progressive disease as the best response to the last line of systemic therapy or stable disease as the best response after at least 2 cycles of the last line of therapy with stable disease duration lasting no longer than 6 months from the last dose of the last line of systemic therapy.
    - Relapsed disease is defined as disease that responded partially or completely to the last line of therapy and has since progressed.
    - Progressive disease must be defined radiologically as per RECIST version 1.1 and be based on CT or MR scans. Progressive disease cannot be defined on just an increased SUV on a PET scan; in such a circumstance, RECIST version 1.1 criteria for progressive disease must be met.
    - Neither radiotherapy nor steroids can be counted as a line of therapy.
- patient has been previously treated for MCL with one of the following cytotoxic chemotherapy regimens: an anthracycline-containing regimen or a bendamustine-containing regimen or a regimen containing high dose cytarabine with or without cisplatin/carboplatin.
- patient has been previously treated with at least one anti-CD20 monoclonal antibody unless there is clear documentation of the determination of CD20 negative disease

- patient has not had stem cell transplantation (SCT) or has had an autologous or allogeneic SCT
- patient has been previously treated for MCL with a BTK inhibitor (such as ibrutinib or acalabrutinib) and that the patient progressed either during treatment or following discontinuation of the BTK inhibitor
- patient has not previously been treated with an anti-CD19 antibody-drug conjugate or if previously treated with an anti-CD19 antibody-drug conjugate that a biopsy of the relapsed/refractory disease has been done and has been shown to be CD19 positive
- patient does not have known active CNS involvement by the lymphoma
- patient is aged 18 years or older on the date of approval for brexucabtagene autoleucel by the National MCL CAR-T Clinical Panel
- patient has an ECOG performance score of 0 or 1
- patient has sufficient end organ function to tolerate treatment with CAR-T cell therapy
- patient has **either** had no previous therapy with any genetically modified autologous or allogeneic T cell immunotherapy **or** the patient has been treated with doses of genetically modified autologous or allogeneic T cell immunotherapy within an abandoned dosing cohort in a first in human dose-escalation phase I clinical trial.
- prior to infusion of brexucabtagene autoleucel, 4 doses of tocilizumab are available for use in this patient in the event of the development of cytokine release syndrome

- brexucabtagene autoleucel-modified CAR-T cell therapy is to be otherwise used as set out in its Summary of Product Characteristics (SPC)
- approval for the use of brexucabtagene autoleucel has been formally given by the National MCL CAR-T cell Clinical Panel
- following national approval for use of brexucabtagene autoleucel there has been local CAR-T cell multidisciplinary team agreement that this patient continues to have the necessary fitness for treatment and fulfils all the treatment criteria listed here

In addition to the above eligibility criteria, for infusion of CAR-T cell therapy the following must be satisfied:

- patient has an ECOG performance score of 0 or 1 or 2.
- patient has required one of the following bridging therapies in between leucapheresis and CAR-T cell infusion:
    - no bridging therapy at all **or**
    - corticosteroids only **or**
    - ibrutinib monotherapy (only for those patients who previously discontinued a BTK inhibitor without disease progression) **or**
    - chemo(immuno)therapy only **or**
    - radiotherapy only **or**
    - corticosteroids and ibrutinib (only for those patients who previously discontinued a BTK inhibitor without disease progression) only **or**
    - corticosteroids and chemo(immuno)therapy **or**

[redacted]

- chemo(immuno)therapy and radiotherapy ± corticosteroids

3.2 [redacted]

3.3 [redacted] The estimated patient numbers per year for this technology within the Cancer Drugs Fund are:

| | |
|---|---|
| As estimated by the company | Year 1: [redacted]<br>Year 2: [redacted]<br>Year 3: [redacted] |
| As estimated by NICE Resource Impact Assessment team | Year 1: [redacted]<br>Year 2: [redacted]<br>Year 3: [redacted] |

## 4 Area(s) of clinical uncertainty

4.1 The appraisal committee identified the following key areas of uncertainty during the course of the appraisal process:

- Immaturity of progression-free, post-progression and overall survival data,
- Quality of life experienced by long-term survivors
- Age at treatment initiation

4.2 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 Appraisal Document.

## 5 Sources of data collection

### *Primary and secondary sources of data collection*

| | |
|---|---|
| Primary source(s) | ○ Clinical trial (ZUMA-2 NCT02601313) |
| Secondary sources | ○ Systemic Anti-Cancer Therapy (SACT) dataset<br>○ NHS England and NHS Improvement's Blueteq data |

### *Description of sources*

5.1 The primary source of data collection during the managed access period will be the ZUMA-2 clinical trial. [redacted], which may then be analysed and reported confidentiality to NICE. [redacted] However, [redacted] if available, the data will be analysed in line with the trial protocol.

5.2 NHS England and NHS Improvement's Blueteq database captures the Cancer Drugs Fund population. NHS England and NHS Improvement 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 NHS Improvement and Public Health England.

5.3 The Systemic Anti-Cancer Therapy (SACT) dataset, is a mandated dataset as part of the Health and Social Care Information Standards. Public Health England is responsible for the collection, collation, quality-assurance and analysis of this dataset.

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 ZUMA-2 will be the source for the following outcomes:

- 2-year Progression Free Survival (PFS):
- 5-year Overall Survival (OS)

It is anticipated that these outcomes will resolve some of the clinical uncertainty associated with earlier analyses of the ZUMA-2 trial data. For example, the results may:

- Validate Kite's choice of overall survival and progression free survival extrapolation and as a result give more certainty to the ICER estimates in the cost-effectiveness analyses
- Obtain more reliable estimate for excess mortality rate by comparing the 5 year OS data mortality rate with the age and sex matched general population mortality adjusted to represent their excess mortality risk used in the original company submission

### *Other data, including SACT*

6.2 Public Health England will collect the following outcomes through SACT and other population-wide datasets 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 that receive the treatment (infused patients)
- Baseline patient characteristics, including gender, age and performance status
- Overall survival

Note: Public Health England will not collect reasons why any subsequent infusion application was not made following a leucapheresis application.

6.3 NHS England and NHS Improvement's Blueteq™ system will collect the following outcomes:

- Number of applications who apply for leucapheresis
- Number of patients that receive the treatment (infused patients)

## 7 Data analysis plan

### *Clinical trials*

7.1 The following analysis will be conducted:

The two-year follow-up data and five-year follow-up from ZUMA-2 will be analysed in line with the trial protocol. If it is possible, three and four-year follow-up data from ZUMA-2 will be provided.

[redacted]; however, if available, the data will be analysed in line with the trial protocol.

### Other data

7.2 At the end of the data collection period Public Health England will provide a final report for NHS England and NHS Improvement which provide analyses based on NHS England and NHS Improvement's Blueteq™ data and routinely collected population-wide data, including that collected via SACT. The necessary controls are in place to ensure that patient confidentiality is not put at risk. The report will be shared with Kite in advance of the planned review of guidance. 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.

## 8 Ownership of the data

8.1 For all clinical trial data listed above, Kite 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 is facilitated by the Public Health England Office for Data Release. Kite will not have access to the Public Health England patient data, but will receive de-personalised summary data, with appropriate governance controls in place.

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 and NHS Improvement.

8.4 Blueteq's Cancer Drugs Fund system data is owned by NHS England and NHS Improvement. NHS England and NHS Improvement is responsible for implementing Blueteq data collection and generally for the analysis of these data. NHS England and NHS Improvement, however, shares Blueteq data with Public Health England for Cancer Drugs Fund evaluation purposes. That sharing is governed by a data sharing agreement between NHS England and NHS Improvement and Public Health England.

## 9 Publication and provision of reports

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 Public Health England will produce a final report which includes analysis of data collected through SACT and from NHS England and NHS Improvement's Blueteq system. This report will be provided to NHS England and NHS Improvement and Kite at the end of the managed access period. The final report will form part of NHS England and NHS Improvement's submission to the Cancer Drugs Fund guidance review, and will therefore be publicly available at the conclusion of guidance review.

9.3 Public Health England will produce interim reports, which will be shared with NHS England and NHS Improvement, NICE and Kite 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 review.

9.4 Publications of any data from the Public Health England reports is not permitted until after the date of publication of the NICE committee papers (on the NICE website) following the first NICE guidance review committee meeting.

9.5 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.

## 10 Data protection

10.1 The terms of clause 7 (data protection) of the managed access agreement, that apply between NHS England and NHS Improvement

and Kite, 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

## 12. Data collection agreement: version control table

| Date updated | Description of update/changes made |
|---|---|
| September 2023 | Following an update from the company, the generic drug name has been updated from autologous anti-CD19-transduced CD3+ cells (KTE-X19) to brexucabtagene autoleucel |

# Commercial Access Agreement

## Brexucabtagene autoleucel for treating relapsed or refractory mantle cell lymphoma [TA677]

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