Managed Access Agreement

Elranatamab for treating relapsed and refractory multiple myeloma after 3 or more treatments (TA1023)

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Elranatamab for treating relapsed and refractory multiple myeloma after 3 or more lines of treatment (TA1023)

Company name: Pfizer Ltd

Primary source of data collection: MagnetisMM-3 (Study Of Elranatamab (PF-06863135) Monotherapy in Participants With Multiple Myeloma Who Are Refractory to at Least One PI, One IMiD and One Anti-CD38 mAb)

Secondary sources of data collection: Systemic Anti-Cancer Therapy (SACT) data set. NHSE's Blueteq data, and IG Database (MDSAS).

NICE Agreement Manager	[redacted]
NHSE Agreement Manager	[redacted]
NHSE Agreement Manager	[redacted]
[Pfizer Ltd] Agreement Manager	[redacted]

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 Elranatamab for treating relapsed and refractory multiple myeloma after 3 or more lines of treatments as defined in 3.1 below and which must have included an immunomodulatory drug, a proteasome inhibitor and an ant-CD38 antibody and when the myeloma has progressed on the last treatment [TA1023]. 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 the publication of the managed access agreement.

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

End of data collection (primary source)	MagnetisMM-3 estimated end date 31st December 2025.
Data available for development of company submission	[redacted]
Anticipated company submission to NICE for a guidance update	July 2026

2.3 Pfizer Ltd. 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 July 2026.

2.4 Pfizer Ltd. acknowledge its 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 guidance update 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 follow the process and methods applicable to guidance updates that are in place at the time the invitation to participate in the guidance update is issued. These may be different from the process and methods applicable to guidance updates when this technology entered into the managed access agreement.

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. This assumes that the data collection period ends as planned and the guidance update follows the standard timelines.

2.8 The company is responsible for paying all associated charges for a guidance update. Note that this includes the 'change fee' if the Company does not provide sufficient notice to NICE regarding changes to the evaluation timelines. Please refer to the NICE website and Charging Procedure for further information.

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 earlier than the estimated dates for data collection, for example, due to earlier than anticipated reporting of an ongoing clinical trial, the company should note:

- Where capacity allows, NICE will explore options to reschedule the guidance update 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).

2.12 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.
- 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 NHSE to provide data over the extended period.

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

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

2.15 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 elranatamab in the Cancer Drugs Fund include:

- The application for elranatamab monotherapy is both being made by and the first cycle of systemic anti-cancer therapy with elranatamab will be prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy.
- The patient is an adult with a proven diagnosis of multiple myeloma.

  Note: patients with amyloidosis or POEMS syndrome are not eligible for elranatamab.
- Elranatamab is not funded for amyloidosis patients (with the exception of patients who have a proven diagnosis of myeloma with an associated diagnosis of amyloidosis) and that NHS funding for elranatamab is only for the relapsed or refractory myeloma indication in the specific indication recommended by NICE.
- Patient has been previously treated with at least one proteasome inhibitor.
- Patient has been previously treated with at least one immunomodulatory agent.
- It will be recorded whether the patient has previously received a pomalidomide-containing regimen or not.
- Patient has previously been treated with at least one anti-CD38 antibody.
- Patient has received at least 3 lines of treatment according to the definition below and also set out below which line of myeloma therapy elranatamab is being used for.

Numbering of a line of treatment is in accordance with the International Myeloma Workshop Consensus recommendations for the uniform reporting of clinical trials (http://doi.org/10.1182/blood-2010-10-299487). 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.

- Clinician is requested to record at which line of therapy elranatamab is being given.

- Patient has NOT been previously treated with any bispecific antibody targeting both BCMA and CD3 unless elranatamab needs to be continued following access to elranatamab via a company compassionate access scheme AND all treatment criteria on this form are fulfilled.

  Note: patients previously treated with any bispecific antibody targeting BCMA and CD3 (e.g. teclistamab) are not eligible for elranatamab.

- Clinician to record whether the patient has ever been treated with a CAR-T therapy such as idecabtagene vicleucel or ciltacabtagene autoleucel.

- Clinician to record whether the patient has been treated with a BCMA-targeted antibody drug conjugate (such as belantamab mafodotin).
- Patient has had progressive disease during or following the last received line of systemic anti-myeloma therapy.
- Clinician confirms and records whether the patient has an ECOG performance status of 0 or 1 or 2.
- Elranatamab will be used as monotherapy only.

  Note: elranatamab is not to be used in combination with any other anti-myeloma agent.
- Clinician confirms that they are aware of: a) the 2 step up doses of elranatamab for the cycle 1 day 1 and cycle 1 day 4 treatments with elranatamab before the patient is then treated with the recommended full elranatamab weekly dosing schedule, and b) the need for patients to switch to 2-weekly elranatamab dosing after 24 weeks of treatment.
- Clinician confirms that the treating hospital has facilities to manage severe reactions to elranatamab including cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS).
- Clinician confirms that they and the treating team are aware of the risks and grading of both cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome, their monitoring and management as illustrated in Tables 2 and 3 of section 4.2 of the elranatamab Summary of Product Characteristics and both I and the treating team have all undergone training in these clinical issues.
- Clinician confirms that clear arrangements have been made for the patient to be monitored for signs and symptoms of toxicities including

CRS and ICANS for 48 hours after administration of the 2 step up doses in week 1 of elranatamab treatment and the patient has been instructed to remain within close proximity of a healthcare facility for these 48 hour periods following treatment on both week 1 day 1 and week 1 day 4.

- Clinician confirms that 1 dose of tocilizumab is immediately available should tocilizumab be required for the treatment of cytokine release syndrome and access to an additional dose of tocilizumab within 8 hours of the previous tocilizumab dose must be ensured.

- Clinician confirms that they are aware that serum immunoglobulin levels require monitoring and treatment with SC or IV immunoglobulin should be considered according to NHS England's Clinical Commissioning Policy 2024 version 2.0.

- Clinician confirms that they are aware of the risk of infections in patients treated with elranatamab and that prophylactic antimicrobials and antivirals should be administered according to local institutional guidelines, as stated in section 4.4 of elranatamab's Summary of Product Characteristics.

- Clinician confirms that the patient will be treated with elranatamab until loss of clinical benefit or the occurrence of excessive toxicity or the withdrawal of patient consent, whichever is the sooner.

  Note: once elranatamab is electively stopped (i.e. for reasons other than temporary toxicity), it cannot be re-started.

- Clinician confirms that a formal medical review as to how elranatamab is being tolerated and whether treatment with elranatamab should continue or not will be scheduled to occur at least by the end of the first 6 weeks of treatment.

- Clinician confirms that when a treatment break of more than 6 weeks beyond the expected weekly or 2-weekly cycle length (as appropriate) is needed, a treatment break approval form will be completed to restart treatment.

- Clinician confirms that elranatamab will be otherwise used as set out in its Summary of Product Characteristics (SPC).

3.2 A free of charge scheme was in place in England and Wales. This scheme commenced in February 2024 and closed on June 30th 2024.

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

As estimated by the company	2024(May/June) - April 2025: 227 (Pro rata,190) April 2025 - April 2026: 302 April 2026 - March 2027: 347 (Pro-rata)
As estimated by the NICE Resource Impact Assessment team	Year 1 – 631 Year 2 – 635 Year 3 – 639

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. long-term OS data for elranatamab
2. long-term PFS data for elranatamab
3. long-term data on IVIg use for elranatamab
4. long-term data on duration of IVIg use for elranatamab
5. improved indirect comparison between elranatamab and POM + DEX and SEL + DEX through additional data collection.

5.2 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.

6 Sources of data collection

Primary and secondary sources of data collection

Primary source(s)	○ **MagnetisMM-3 (**Study Of Elranatamab (PF-06863135) Monotherapy in Participants With Multiple Myeloma Who Are Refractory to at Least One PI, One IMiD and One Anti-CD38 mAb**)**
Secondary sources	○ Systemic Anti-Cancer Therapy (SACT) dataset ○ NHSE's Blueteq data ○ IG database (MDSAS)

Description of sources

6.1 MagnetisMM-3 is an open label, multicenter, non-randomised, phase 2 study of elranatamab (PF-06863135) monotherapy in participants with multiple myeloma who are refractory to at least one proteasome inhibitor (PI), one immunomodulatory drug and one anti-CD38 antibody. The purpose of the study is to evaluate whether single-agent elranatamab (PF-06863135) can provide clinical benefit in participants with relapsed/refractory multiple myeloma. Elranatamab is a bispecific antibody: binding of elranatamab to

CD3-expressing T-cells and BCMA-expressing multiple myeloma cells causes targeted T-cell-mediated cytotoxicity.

6.2 Reported outcomes include progression free survival (PFS), overall survival (OS), objective response rate (ORR), complete response rate (CRR), duration of response (DOR), Time to response (TTR), along with adverse events (AEs), health-related quality of life (HRQoL) and time to treatment discontinuation (TTD).

Further information can be found on MagnetisMM-3 - ClinicalTrials.gov

6.3 NHSE's Blueteq database captures the Cancer Drugs Fund population. The lawfulness of this processing is covered under article 6(1)e of the United Kingdom General Data Protection Regulations (GDPR) (processing is necessary for the performance of a task carried out in the public interest or in the exercise of official authority vested in the controller). NHSE, through the National Disease Registration Service (NDRS), does have statutory authority to process confidential patient information (without prior patient consent) afforded through the NDRS Directions 2021 issued to it by the Secretary of State for Health and Social Care and has issued the NDRS Data Provision Notice under section 259 of the Health and Social Care Act 2012 regarding the collection of the Blueteq data from NHSE.

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

6.5 Datasets collected and collated by NDRS in NHSE will be the secondary source of data collection.

7 Outcome data

Clinical trial

7.1 The following outcomes, which will help to reduce the uncertainties identified by the NICE committee, are planned to be collected in the ongoing MagnetisMM-3 trial. The key outcome data to be collected includes;

- Progression free survival (PFS)
- Overall survival (OS)
- Time to treatment discontinuation (TTD)
- Intra venous immunoglobulin (IVIG) replacement

The data collected will help resolve the uncertainty around longer term extrapolations of survival outcomes and resource use. At study completion the length of follow up will be approximately 44 months which is substantially longer than the 15-month data cut presented at the time of submission where both median PFS and OS were not reached and the study was subject to censoring.

Other data, including SACT

7.2 NDRS in NHSE will collect the following outcomes through SACT unless it is determined by the SACT Operational Group that no meaningful data will be captured during the period of data collection. NHSE will also collect data from IG database (MDSAS) on levels of IVIG in this population:

- Number of patients starting treatment (SACT)
- Baseline patient characteristics, including gender, age and performance status (SACT)
- Treatment duration (SACT)

- Overall survival (SACT)
- Dosing
- IVIG use in patients receiving elranatamab (IG Database)

7.3 NHSE's Blueteq system will collect the following outcomes:

- Number of applications to start treatment
- Numbers of patients who have received prior CAR-T treatment prior to elranatamab
- Numbers of patients who have received prior BCMA-directed ADC prior to elranatamab

8 Data analysis plan

Clinical trials

8.1 The final analysis of MagnetisMM-3 is due to be performed after the final overall survival event and will follow the analysis plan outlined in the trial protocol (due approximately by 31 December 2025). The data used to address the uncertainties will align to Cohort A from MagnetisMM-3. MagnetisMM-3 enrolled 2 independent parallel cohorts;

- Cohort A: Patients who had not received any prior BCMA-directed therapy (BCMA-naïve; n = 123)
- Cohort B: Patients who had previously received BCMA-directed ADC or BCMA-directed CAR-T therapy, either approved or investigational (BCMA-exposed; n = 64)

8.2 No BCMA-targeted therapies are currently reimbursed for use in the UK; therefore, Cohort A (BCMA-naïve) is the most relevant patient population and is the focus of this submission.

The trial protocol and statistical analysis plan along with further information is available at MagnetisMM-3 - ClinicalTrials.gov

8.3 Subsequent to the NICE submission there has been a further restricted data cut available as of November 2023 with a full data cut planned with data available for use from end of [redacted].

8.4 The database lock will occur once the last follow up event has occurred, which is expected in December 2025. The data will be available for the development of a company submission in July 2026.

Other data

8.5 At the end of the data collection period NHSE will provide a final report which provide analyses based on NHSE's Blueteq data and routinely collected population-wide data, including that collected via SACT. The necessary controls will be put in place to ensure that patient confidentiality is not put at risk. The report will be shared with the company in advance of the planned guidance update. 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.

9 Ownership of the data

9.1 For all clinical trial data listed above, Pfizer Inc. will be the owner

9.2 There are new or additional data governance requirements for ongoing clinical trials or routine NHSE data collection.

9.3 This work uses data that has been provided by patients and collected by the NHS as part of their care and support. The data are collated, maintained and quality assured by the National Disease Registration Service, which is part of NHSE. The company will not have access to the

NHSE patient data, but will receive de-personalised summary data, with appropriate governance controls in place.

9.4 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 NHSE, have been established with NHS Trusts and NHSE.

9.5 Blueteq's Cancer Drugs Fund system data is owned by NHSE. NHSE is responsible for implementing Blueteq data collection and generally for the analysis of these data. The lawfulness of this processing is covered under article 6(1)e of the United Kingdom General Data Protection Regulations (UK GDPR) (processing is necessary for the performance of a task carried out in the public interest or in the exercise of official authority vested in the controller). NHSE, through the National Disease Registration Service, does have statutory authority to process confidential patient information (without prior patient consent) afforded through the National Disease Registries (NDRS) Directions 2021 issued to it by the Secretary of State for Health and Social Care. The lawfulness of NHSE's processing is covered under article 6(1)(c) of the UK GDPR – processing is necessary for compliance with a legal obligation to which the controller is subject (the NDRS Directions).

10 Publication

10.1 The details/authorship of any proposed publications arising from these studies will be planned with the publication of the final study results.

10.2 NDRS will produce a final report which includes analysis of data collected through SACT and from NHSE's Blueteq system. This report will be provided to NHSE and the company at the end of the managed access period. The final report will form part of NHSE's submission to the guidance update, and will therefore be publicly available at the conclusion of the guidance update.

10.3 NDRS will produce interim reports, which will be shared with NICE and the company 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 update.

10.4 Publications of any data from the NDRS reports is not permitted until after the date of publication of the NICE committee papers (on the NICE website) following the first NICE guidance update committee meeting.

10.5 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.

11 Data protection

The terms of clause 7 (data protection) of the managed access agreement, that applies between NHSE and Pfizer 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.

12 Equality considerations

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