Managed Access Agreement

Fedratinib for treating disease-related splenomegaly or symptoms in myelofibrosis [ID1501]

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cancer Drugs Fund – Data Collection Arrangement

Fedratinib for treating disease-related splenomegaly or symptoms in myelofibrosis [ID1501]

Company name: Bristol Myers Squibb Pharmaceuticals Ltd

Primary source of data collection: FREEDOM 2

Secondary source of data collection: NHS Digital routine population-wide cancer data sets, including Systemic Anti-Cancer Therapy data set

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NHSE&I Agreement Manager	Prof Peter Clark, CDF Clinical Lead
NHS Digital Agreement Manager	Martine Bomb, Head of Data Projects
Bristol Myers Squibb Agreement Manager	Scott Cooke, General Manager UK&I

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 fedratinib for treating disease-related splenomegaly or symptoms in myelofibrosis [ID1501] (to be updated with TA number after final guidance has been published). 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	February 2023

2.3 Bristol Myers Squibb 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 2023.

2.4 Bristol Myers Squibb 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 The company is responsible for paying all associated charges for a Cancer Drugs Fund review. Further information is available on the NICE website.

2.8 The company must inform NICE and NHS England and NHS Improvement (NHSE&I) in writing 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 NHSE&I.

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, the company 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, the company should note:

- The company must submit a written request to NICE and NHSE&I, 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 NHS Digital to provide data over the extended period.

2.12 Bristol Myers Squibb acknowledge their responsibility to provide an evidence submission for this technology to NICE under all circumstances following a period of managed access.

2.13 In the event that Bristol Myers Squibb do not make a submission to NICE for the purpose of updating the guidance, NICE and NHSE&I will require the company 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&I, 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. The presentations from this engagement event will be published on the NICE website.

2.14 NICE and NHSE&I 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 fedratinib in the Cancer Drugs Fund include:

- application is being made by and the first cycle of systemic anti-cancer therapy with fedratinib will be prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy
- patient has primary myelofibrosis (also known as chronic idiopathic myelofibrosis) or post-polycythaemia vera myelofibrosis or post-essential thrombocythaemia myelofibrosis
- patient's myelofibrosis has a risk category that is either intermediate-2 or high risk
- patient has symptomatic disease-related splenomegaly and/or constitutional symptoms of myelofibrosis
- patient has been previously treated with ruxolitinib
- patient has an ECOG performance status (PS) of 0 or 1 or 2

- patients must have thiamine (vitamin B1) levels tested both before and during fedratinib therapy and that thiamine deficiency must be corrected before treatment starts and during fedratinib therapy
- patient has not previously received fedratinib unless the patient has received fedratinib via a company early access scheme and the patient meets all the other criteria listed here
- fedratinib is to be continued until loss of clinical benefit or unacceptable toxicity or patient choice to stop treatment
- clinician is aware fedratinib has clinically important interactions with drugs which affect the CYP3A4, CYP2C19 and CYP2D6 enzyme systems
- a formal medical review as to how fedratinib is being tolerated and whether treatment with fedratinib should continue or not will be scheduled to occur at least by the start of the third 4-weekly cycle of treatment
- when a treatment break of more than 6 weeks beyond the expected 4-weekly cycle length is needed, I will complete a treatment break approval form to restart treatment, including indicating as appropriate if the patient had an extended break because of COVID 19
- fedratinib is to be otherwise used as set out in its Summary of Product Characteristics

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

As estimated by the company	Year 1 - [redacted] Year 2 - [redacted]

As estimated by NICE Resource Impact Assessment team	Year 1 - [redacted] Year 2 - [redacted] Year 3 - [redacted]

4 Patient safety

4.1 The company and NHSE&I 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&I 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. Whether fedratinib extends overall survival compared to best available therapy

2. Overall survival for those on best available therapy

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)	○ FREEDOM 2
Secondary sources	○ Systemic Anti-Cancer Therapy (SACT) dataset ○ NHSE&I's Blueteq data

Description of sources

6.1 The primary source of additional data will be FREEDOM 2, a multicenter, open-label, randomised study to evaluate the efficacy and safety of fedratinib compared to best available therapy (BAT) in subjects with DIPSS (Dynamic International Prognostic Scoring System)-intermediate or high-risk primary myelofibrosis (PMF), post-polycythemia vera myelofibrosis (post-PV MF), or post-essential thrombocythemia myelofibrosis (post-ET MF) and previously treated with ruxolitinib.

6.2 NHSE&I's Blueteq database captures the Cancer Drugs Fund population. NHSE&I shares Blueteq data with NHS Digital for the Cancer Drugs Fund evaluation purposes. 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). NHS Digital, 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, and has issued the NDRS Data Provision Notice under section 259 of the Health and Social Care Act 2012 regarding collection of the Blueteq data from NHSE&I.

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

6.4 NHS Digital will collect data, including via the SACT dataset, alongside the primary source of data collection.

7 Outcome data

Clinical trial

7.1 The key outcomes to be collected are:

- Overall survival of patients initiated on fedratinib
- Overall survival of patients continuing on best available therapy
- The proportion of patients in best available therapy that are on ruxolitinib
- Spleen volume response

The data from the trial will give direct comparison of key outcomes of fedratinib versus best available therapy.

Other data, including SACT

7.2 NHS Digital 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:

- Number of patients starting treatment
- Baseline patient characteristics, including gender, age and performance status
- Treatment duration
- Overall survival

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

- Number of applications to start treatment

- Risk status of the patients i.e. intermediate-2 or High risk

8 Data analysis plan

Clinical trials

8.1 Final analysis will follow the analysis plan outlined in the trial protocol. No interim analyses are planned prior to database lock.

8.2 Database lock is expected [redacted], with data available to analyse in [redacted].

Other data

8.3 At the end of the data collection period NHS Digital will provide a final report for NHSE&I which provide analyses based on NHSE&I'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 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.

9 Ownership of the data

9.1 For all clinical trial data listed above, Bristol Myers Squibb will be the owner

9.2 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 NHS Digital. The company will not have access to the NHS Digital patient data, but will receive de-personalised summary data, with appropriate governance controls in place.

9.3 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 NHS Digital, have been established with NHS Trusts and NHSE&I.

9.4 Blueteq's Cancer Drugs Fund system data is owned by NHSE&I. NHSE&I is responsible for implementing Blueteq data collection and generally for the analysis of these data. NHSE&I, however, shares Blueteq data with NHS Digital for Cancer Drugs Fund evaluation purposes. 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). NHS Digital, 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 NHS Digital'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 NHS Digital will produce a final report which includes analysis of data collected through SACT and from NHSE&I's Blueteq system. This report will be provided to NHSE&I and the company at the end of the managed access period. The final report will form part of NHSE&I's submission to the Cancer

Drugs Fund guidance review, and will therefore be publicly available at the conclusion of guidance review.

10.3 NHS Digital will produce interim reports, which will be shared with NHSE&I, 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 review.

10.4 Publications of any data from the NHS Digital 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.

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

11.1 The terms of clause 7 (data protection) of the managed access agreement, that apply between NHSE&I and Bristol Myers Squibb, 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

12.1 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.