Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Bosutinib for untreated chronic myeloid leukaemia

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of bosutinib within its marketing authorisation for treating chronic myeloid leukaemia.

Background

Chronic myeloid leukaemia (CML) is characterised by the excessive production of white cell precursors by the bone marrow. Typically, chronic myeloid leukaemia develops and progresses slowly and does not have any symptoms in its early stages. It progresses through 3 phases: the chronic phase, the accelerated phase and the blast crisis phase, with the latter two being grouped together as the advanced phase. The majority of people are diagnosed in the chronic phase, from which they either go through the accelerated phase, or move directly into blast crisis in which the disease transforms into a fatal acute leukaemia.

CML is a rare disease, accounting for less than 1% of all cancer cases[1]. In England in 2014, 631 people were diagnosed with CML[2]. Almost half of all cases of CML are diagnosed in people over 65[3]. A specific chromosomal abnormality known as the 'Philadelphia chromosome' is present in 95% of people with CML[4].

NICE technology appraisal guidance 426 recommends standard dose imatinib, dasatinib and nilotinib as options for untreated, chronic-phase Philadelphia-chromosome-positive CML. NICE technology appraisal guidance 70 also recommends standard dose imatinib for the treatment of people with untreated Philadelphia-chromosome-positive CML who initially present in the accelerated phase or with blast crisis.

The technology

Bosutinib (Bosulif, Pfizer) is a second generation tyrosine kinase inhibitor that inhibits Abl-kinases, including the Bcr-Abl kinsase that promotes CML. It also inhibits the Src family kinases, which have been implicated in driving CML progression. It is administered orally.

Bosutinib does not currently have a marketing authorisation in the UK for untreated chronic myeloid leukaemia. It has been studied in clinical trials in comparison with imatinib, in adults with newly diagnosed chronic-phase Philadelphia-chromosome-positive chronic myeloid leukaemia.

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Bosutinib has a marketing authorisation in the UK for the treatment of adult patients with chronic phase (CP), accelerated phase (AP), and blast phase (BP) Philadelphia chromosome positive chronic myelogenous leukaemia (Ph+ CML) previously treated with one or more tyrosine kinase inhibitor(s) and for whom imatinib, nilotinib and dasatinib are not considered appropriate treatment options.

Intervention(s)	Bosutinib
Population(s)	Adults with newly diagnosed chronic-phase Philadelphia-chromosome-positive chronic myeloid leukaemia
Comparators	• Dasatinib • Standard dose imatinib • Nilotinib
Outcomes	The outcome measures to be considered include: • overall survival • progression and/or event-free survival • response rates • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any patient access schemes for the intervention or comparator technologies will be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the

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	therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: 'Ponatinib for treating chronic myeloid leukaemia and acute lymphoblastic leukaemia' (2017). NICE Technology Appraisal 451. Review date June 2020. 'Dasatinib, nilotinib and imatinib for untreated chronic myeloid leukaemia' (2016). NICE Technology Appraisal 426. Review date December 2019. 'Dasatinib, nilotinib and high-dose imatinib for treating imatinib-resistant or intolerant chronic myeloid leukaemia' (2016). NICE Technology Appraisal 425. Review date December 2019. 'Bosutinib for previously treated chronic myeloid leukaemia' (2016). NICE Technology Appraisal 401. Review date August 2019. 'Guidance on the use of imatinib for chronic myeloid leukaemia' (2003). NICE Technology Appraisal 70. Review date to be confirmed. Related NICE Pathways: Blood and bone marrow cancers (2017) NICE pathway http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers
Related National Policy	NHS England (2017/18) Manual for prescribed specialised services. Chapters 29 Blood and marrow transplantation services (adults and children) and 105 Specialist cancer services (adults) https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual-2.pdf Department of Health (2014) Improving outcomes: a strategy for cancer fourth annual report https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report NHS England (2011) Improving outcomes: a strategy for cancer https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213785/dh_123394.pdf Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2. https://www.gov.uk/government/publications/nhs-

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	outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for bosutinib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for untreated chronic myeloid leukaemia?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom bosutinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider bosutinib will fit into the existing NICE pathway for blood and bone marrow cancers?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which bosutinib will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider bosutinib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of bosutinib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

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To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

[1] Cancer Research UK Chronic myeloid leukaemia (CML) statistics. Accessed October 2017
[2] Cancer Research UK Chronic myeloid leukaemia (CML) statistics. Accessed October 2017
[3] Cancer Research UK Chronic myeloid leukaemia (CML) statistics. Accessed October 2017
[4] Macmillan Cancer Support Chronic myeloid leukaemia (CML). Access October 2017.

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