NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Asciminib for chronic myeloid leukaemia after two or more tyrosine kinase inhibitors

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of asciminib within its marketing authorisation for treating Philadelphia-chromosome-positive chronic myeloid leukaemia (CML) in the chronic phase after two or more tyrosine kinase inhibitors.

Background

CML is a type of cancer that affects the blood-forming cells, called myeloid cells, found in the bone marrow[1,2]. People with CML have a genetic mutation in their bone marrow cells which causes an abnormal chromosome to form, known as the Philadelphia chromosome[1]. The Philadelphia chromosome is made up of 2 genes which join to make a single fusion gene called BCR-ABL[1]. The BCR-ABL gene causes the myeloid cells to produce a protein, called tyrosine kinase, that encourages white blood cells to grow and multiply[1]. CML usually develops and progresses slowly. It is diagnosed in one of three distinct phases; chronic, accelerated or blast phase [3].

The incidence of CML is approximately 1.3 per 100,000 in the UK [4], it is a rare condition with around 760 people diagnosed in the UK each year [4]. The median age at diagnosis is between 60 and 65 years of age. Around 90% of CML cases are diagnosed at the chronic phase [2]. It is estimated that there are approximately 645 patients in the UK eligible for third line CML treatment.

NICE guidance exists on the following: ponatinib for previously treated chronic myeloid leukaemia and acute lymphoblastic leukaemia (TA451), dasatinib, nilotinib and high-dose imatinib for treating imatinib-resistant or intolerant chronic myeloid leukaemia (TA425), and bosutinib for previously treated chronic myeloid leukaemia (TA401).

The technology

Asciminib (ABL001, Novartis) is an allosteric inhibitor of the tyrosine kinase BCR-ABL1 fusion protein. It binds to BCR-ABL1, which inhibits BCR-ABL1 mediated cell proliferation. It is administered orally.

Asciminib does not currently have marketing authorisation in the UK for previously treated Philadelphia chromosome-positive CML. It has been studied in clinical trials in comparison with bosutinib in adults with CML in the chronic phase; previously treated with 2 or more tyrosine kinase inhibitors.

Intervention(s)	Asciminib
Population(s)	Adults with chronic-phase Philadelphia chromosome-positive chronic myeloid leukaemia previously treated with 2 or more tyrosine kinase inhibitors
Comparators	• Bosutinib • Dasatinib • Imatinib • Nilotinib • Ponatinib
Outcomes	The outcome measures to be considered include: • major molecular response (MMR) • progression-free survival (PFS) • overall survival (OS) • response rates • time to response • disease progression • 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. 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.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the 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	Ponatinib for treating chronic myeloid leukaemia and acute lymphoblastic leukaemia (2017) NICE technology appraisal

and NICE Pathways	guidance 451 Dasatinib, nilotinib and high-dose imatinib for treating imatinib-resistant or intolerant chronic myeloid leukaemia (2016) NICE technology appraisal guidance 425 Bosutinib for previously treated chronic myeloid leukaemia (2016) NICE technology appraisal guidance 401 Myeloid leukaemia (2021) NICE pathway https://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers#path=view%3A/pathways/blood-and-bone-marrow-cancers/myeloid-leukaemia.xml&content=view-node%3Anodes-ponatinib
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) : Chapter 29 Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1,2 and 3. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for asciminib been included in the scope?

Which treatments are established clinical practice in the NHS for previously treated PH+ chronic myeloid leukaemia?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom asciminib is expected to be more clinically effective and cost effective or other groups that should be examined separately? OR Are the subgroups suggested in 'other considerations appropriate?

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

Where do you consider asciminib will fit into the existing NICE pathway for Myeloid leukaemia?

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 asciminib 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 asciminib 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 CML)?

Do you consider that the use of asciminib 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.

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. Hochhaus, A., Saussele S., Rosti G., Mahon F. X., Janssen J. J. W. M., Hjorth-Hansen H., et al. *Chronic myeloid leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up*. Annals of oncology : official journal of the European Society for Medical Oncology. 2017;28(suppl_4):iv41-iv51. Available from: https://10.1093/annonc/mdx219
2. Leukaemia Foundation. *Chronic myeloid leukaemia (CML).* 2021. Available from: https://www.leukaemia.org.au/disease-information/leukaemias/chronic-myeloid-leukaemia/ [Accessed 16 April 2021].
3. Cancer Research UK. *Chronic myeloid leukaemia (CML): Stages.* 2020. Available from: https://www.cancerresearchuk.org/about-cancer/chronic-myeloid-leukaemia-cml/stages [Accessed 27 April 2021].
4. Cancer Research UK. *Chronic myeloid leukaemia (CML) incidence statistics*. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/leukaemia-cml/incidence [Accessed 16 April 2021].