National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Asciminib for treating chronic myeloid leukaemia after 2 or more tyrosine kinase inhibitors [ID3813]

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Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	Leukaemia Care	-	No change required.
	Novartis Pharmaceuticals UK Ltd	-	No change required.
Wording	Leukaemia Care	Yes	Thank you for your comment. No changes required.
	Novartis Pharmaceuticals UK Ltd	The current wording of the draft remit appropriately reflects the use of asciminib, according to its potential marketing authorisation.	Thank you for your comment. No changes required.
Timing Issues	Leukaemia Care	N/A	No change required.
	Novartis Pharmaceuticals UK Ltd	-	No change required.

Section	Consultee/ Commentator	Comments [sic]	Action
Additional comments on the draft remit	Leukaemia Care	-	No change required.
	Novartis Pharmaceuticals UK Ltd	N/A	No change required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Leukaemia Care	N/A	No change required.
	Novartis Pharmaceuticals UK Ltd	The Background section as currently written is generally accurate, with the exception of the last statement in the second paragraph. It is not clear from the text whether the number of patients presented (n=645) represents the prevalence or incidence of the 3rd line CML in a given year. If a prevalence figure, we believe this is an underestimate of the population. Based on an analysis of the Haematological Malignancy Research Network (HMRN) registry, [redacted] Assuming the study population is generalisable to the UK, an estimate of the population eligible for 3L+ treatment would be in the region of 1500-2000 patients.	Thank you for your comments. The background section is intended to provide a brief summary of the disease. Reference to prevalence figures have been removed for clarity.
The technology/ intervention	Leukaemia Care	Yes	Thank you for your comments. No changes required.
	Novartis Pharmaceuticals UK Ltd	To be more accurate in this section, we recommend replacing the first paragraph by the following: “Asciminib is the first-in-class STAMP (Specifically Targeting the ABL Myristoyl Pocket) inhibitor. It is distinct from approved ABL1 kinase inhibitors in that it does not bind to the ATP-binding site of the kinase. It 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.”	Thank you for your comments. The technology section is intended to provide a brief description of the mechanism of action. No changes required.

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Population	Leukaemia Care	The population should include both those adults with chronic-phase Philadelphia chromosome-positive chronic myeloid leukaemia who are on 3rd line treatment due to either intolerance or resistance to previous TKI treatments. We are also aware of asciminib trials in other indications (including 1st line) so future licensing may be broader than the draft remit, though these may be addressed through subsequent NICE appraisals.	Thank you for your comments. The population described in the scope is broad enough to capture both of these populations, therefore changes to the scope is not required. NICE can only appraise technologies within their marketing authorisation, and therefore any changes to the marketing authorisation may be addressed in future appraisals.
	Novartis Pharmaceuticals UK Ltd	The Population section correctly defines the target population. The current evidence demonstrates the clinical and cost effectiveness of asciminib in the population of interest – people with CML previously treated with two or more TKIs. We do not believe there are any important subgroups within the anticipated licensed population which warrant specific consideration.	Thank you for your comments. No changes required.
Comparators	Leukaemia Care	Most patients are likely to have tried imatinib and nilotinib/dasatinib prior to 3rd line treatment making Bosutinib and Ponatinib more appropriate comparators at this stage.	Thank you for your comments. Imatinib has been removed from the list of comparators.

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		We do not have the data of the exact number of patients who have received each TKI in NHS clinical practice. However, imatinib in particular is unlikely to be a relevant comparator in this setting.	Section 2.2.4 , NICE's Guide to the methods of technology appraisal 2013 states that at the scoping stage of the appraisal, identification of comparators should be inclusive. As it is unclear how many people receive nilotinib or dasatinib as a third-line treatment, these comparators have not been removed from the scope.
	Novartis Pharmaceuticals UK Ltd	We believe all comparators listed in the draft scope are appropriate, with the exception of imatinib, which we do not believe is a relevant comparator in this appraisal. Imatinib is mainly used as a first line treatment in CML – based on an analysis of the HMRN registry, 89.9% of the newly diagnosed CML patients receive imatinib. It is also not recommended for later lines CML patients, based on NICE guidance (TA425) that stated "high-dose imatinib is not recommended for treating CML patients who are imatinib-resistant" Imatinib was also not considered to be a relevant comparator to bosutinib in TA401 and to ponatinib in TA451. Hence, we do not believe imatinib to be a relevant comparator for ≥third-line treatment with asciminib.	Thank you for your comments. Imatinib has been removed from the list of comparators.

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Outcomes	Leukaemia Care	Another key outcome would be the proportion of patients achieving treatment-free remission (TFR).	Thank you for your comments. The list of outcomes are examples and not intended to be an exhaustive list. Outcomes in the scope are meant to capture outcomes relevant to patients and not necessarily those in the trial. Major molecular response has been deleted as an outcome from the scope. Disease progression has also been deleted from the list of outcomes in the scope, as this can be captured through the analyses of progression-free survival and overall survival.
	Novartis Pharmaceuticals UK Ltd	We agree that the listed outcome measures are relevant and important to consider. However, we also consider time to treatment discontinuation (TTD) as an important treatment outcome and recommend including it.	Thank you for your comments. The list of outcomes are examples and not intended to be an exhaustive list.

Section	Consultee/ Commentator	Comments [sic]	Action
			Outcomes in the scope are meant to capture outcomes relevant to patients and not necessarily those in the trial. Major molecular response has been deleted as an outcome from the scope. Disease progression has also been deleted from the list of outcomes in the scope, as this can be captured through the analyses of progression-free survival and overall survival.
Economic analysis	Leukaemia Care	N/A	Thank you for your comments. No changes required.
	Novartis Pharmaceuticals UK Ltd	Our submission will follow the NICE reference case.	Thank you for your comments. No changes required.
Equality and Diversity	Leukaemia Care	N/A	Comment noted. No changes required.

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	Novartis Pharmaceuticals UK Ltd	We do not believe that there are equality issues.	Thank you for your comments. No changes required.
Other considerations	Leukaemia Care	N/A	No changes required.
	Novartis Pharmaceuticals UK Ltd	None	No changes required.
Innovation	Leukaemia Care	Asciminib addresses an unmet need in the treatment of CML. We would argue that the new mechanism of action of asciminib (targeting the ABL myristoyl pocket) makes it innovative.	Thank you for your comments. The committee will consider the extent to which asciminib is innovative during the development of the appraisal. No changes required.
	Novartis Pharmaceuticals UK Ltd	While newly diagnosed CML patients may be offered several treatment options, a proportion of patients develop resistance or intolerance to first-/second-line treatments. Thus, there is a clinical need for alternative later-line therapy options. Unlike other TKIs, asciminib has a novel mechanism of action. It is specifically targeting the ABL myristoyl pocket (STAMP). This may overcome resistance due to mutations in the ATP binding site. It has also been demonstrated to improve the tolerability profile of asciminib compared to other TKIs.	Comment noted. The committee will consider the extent to which asciminib is innovative during the development of the appraisal. No changes required.

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NICE Pathways [	Leukaemia Care	N/A	No changes required.
	Novartis Pharmaceuticals UK Ltd	N/A	No changes required.
Questions for consultation	Leukaemia Care	N/A	No changes required.
	Novartis Pharmaceuticals UK Ltd	***Any barriers to adoption of this technology into practice?*** We do not anticipate any barriers to asciminib's adoption into clinical practice. [redacted] **Would it be appropriate to use the cost comparison methodology for this topic?** No, the cost comparison method is not appropriate for this appraisal, as we are not aware of other comparators' PAS. A cost-utility analysis will be submitted as part of our evidence. ***Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?*** Unlike its comparators, asciminib would provide CML patients with a treatment which offers an improved tolerability profile, and a potentially more effective treatment option. As a result, there would be an expected impact on patients' quality of life and NHS resource use. ***Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?*** Yes	Thank you for your comments. No changes required. Thank you for your comment. No changes required. Thank you for your comments. No changes required. Thank you for your comment. No changes required.

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		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? No, we are not anticipating any substantial new evidence for comparators.	Thank you for your comment. No changes required.
Additional comments on the draft scope	Leukaemia Care	-	No changes required.
	Novartis Pharmaceuticals UK Ltd	-	No changes required.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

None.