National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Ribociclib in combination with an aromatase inhibitor for previously untreated advanced or metastatic hormone receptor-positive, HER2-negative breast cancer
Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Wording	Breast Cancer Now	Yes, to the best of our knowledge	Thank you for your comment.
	Novartis Pharmaceuticals UK Ltd	Yes	Thank you for your comment.
Timing Issues	Breast Cancer Now	This treatment could be an important treatment option for patients with hormone-positive breast cancer, so an appraisal should be done in a timely way.	Thank you, comment noted.
	Novartis Pharmaceuticals UK Ltd	There is urgency for this appraisal as there are currently limited treatment options for Advanced Breast Cancer patients who are hormone receptor-positive, HER2-negative. Clinical data from MONALEESA-2 trial demonstrates clinical significant and relevant delay in disease progression compared with current standard of care Letrozole.	Thank you, comment noted.

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		Ribociclib is expected to gain a UK Marketing Authorisation in [redacted] and Novartis believes a timely appraisal should occur in line with the new NICE process timelines.	

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Breast Cancer Now	The background information is correct, but we note that the following two facts are taken from local data, which may not be representative of the whole patient population: • The 5-year survival rate for people with metastatic breast cancer in England is 15% • around 35% of people with early or locally advanced disease will progress to metastatic breast cancer in the 10 years following diagnosis	Thank you, comment noted. The background section has been changed.
	Novartis Pharmaceuticals UK Ltd	It should be noted that the number of females diagnosed with breast cancer was 48,957 for England and Wales in 2014 (http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/incidence-invasive#collapseZero) It should be noted that the number of female deaths from breast cancer was 10,074 for England and Wales in 2014 (http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/mortality#heading-Zero)	Comment noted. The figures in the scope relate to England only.

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The technology/ intervention	Breast Cancer Now	In the technology section, the document says: “When these two proteins are activated they can cause the cancer cells to grow and divide too quickly.” As far as we are aware, the activation of either one of these proteins can cause cancer. Ribociclib works by targeting both of the proteins.	Thank you, comment noted. The scope has been amended.
	Novartis Pharmaceuticals UK Ltd	No additional comments	No action required.
Population	Breast Cancer Now	This is correct, to the best of our knowledge.	Thank you, comment noted.
	Novartis Pharmaceuticals UK Ltd	The population defined is appropriate and there are no subgroups that should be considered separately	Thank you, comment noted.
Comparators	Breast Cancer Now	Aromatase inhibitors are currently the standard treatment for hormone-positive women who get diagnosed with metastatic breast cancer.	Thank you, comment noted.
	Novartis Pharmaceuticals UK Ltd	Agreed. As proposed in the draft scope, the current standard of care for first-line advanced or metastatic hormone receptor-positive, HER2-negative breast cancer is endocrine therapy, of which are aromatase inhibitors (letrozole and anastrazole)	Thank you, comment noted.
Outcomes	Breast Cancer Now	We believe that these outcomes do capture the most important health benefits for patients.	Thank you, comment noted.

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	Novartis Pharmaceuticals UK Ltd	No additional comments	No action required.
Economic analysis	Breast Cancer Now	No comment	No action required.
	Novartis Pharmaceuticals UK Ltd	The economic analysis will adopt a lifetime time horizon	Thank you, comment noted.
Equality and Diversity	Breast Cancer Now	No equality issues are present, to the best of our knowledge	Thank you, comment noted.
	Novartis Pharmaceuticals UK Ltd	No comments	No action required.
Innovation	Breast Cancer Now	This treatment will work in a similar way to palbociclib, which is a drug currently being appraised by NICE. Both of these drugs are innovative in their function and could give precious extra time to patients with an incurable type of breast cancer, before their disease progresses.	Thank you, comment noted.
	Novartis Pharmaceuticals UK Ltd	Yes. Ribociclib is an orally bioavailable, selective, small-molecule inhibitor of Cyclin-dependent kinases (CDK4/6) inhibitor which is a new class of therapy in the management of advanced breast cancer. The aim is to selectively interrupt cell-cycle regulation in cancer cells by interfering with CDK action.	Thank you, comments noted. Innovation will be discussed further at appraisal stage.

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		Ribociclib is a selective CDK4/6 inhibitor with a novel mechanism of action that blocks cell proliferation and cellular DNA synthesis by preventing cell-cycle progression from G1 to S phase by preventing RB phosphorylation The efficacy observed in patients treated with ribociclib, together with its tolerable toxicity profile, represents a step-change in the management of women with metastatic breast cancer. Results from the pivotal phase III clinical trial (MONALEESA-2) have demonstrated a significantly longer duration of progression-free survival (PFS) for ribociclib in combination with letrozole when compared to placebo plus letrozole. Reference published data: Hortobagyi GN, et al. N Engl J Med. 2016 Nov 3;375(18):1738-1748	
Other considerations	Breast Cancer Now	None.	No action required.
	Novartis Pharmaceuticals UK Ltd	No comments.	No action required.
Questions for consultation	Breast Cancer Now	We would expect ribociclib to fit within the advanced breast cancer pathway	Thank you, comment noted.

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	Novartis Pharmaceuticals UK Ltd	***Have all relevant comparators for ribociclib been included in the scope?*** Yes. ***Which treatments are considered to be established clinical practice in the NHS for untreated advanced oestrogen-receptor positive, HER2-negative breast cancer in postmenopausal women?*** Treatments which are considered established clinical practice for advanced oestrogen-receptor positive, HER2-negative breast cancer are aromatase inhibitors, letrozole and anastrozole. As highlighted above, there is evidence that chemotherapy is used for first-line treatment in a wider population than recommended in clinical guidelines. **Are the outcomes listed appropriate?** Yes. **Are there any subgroups of people in whom ribociclib is expected to be more clinically effective and cost effective or other groups that should be examined separately?** No. ***Where do you consider ribociclib will fit into the existing NICE pathways Advanced breast cancer [2015])?*** Ribociclib in combination with an aromatase inhibitor should be considered as a first-line treatment within its expected marketing authorisation:	Thank you, comments noted. It was agreed at the palbocilib scoping workshop that chemotherapy was not a comparator for these patients.

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		• in combination with letrozole is indicated for the treatment of postmenopausal women with hormone receptor-positive, HER2-negative advanced or metastatic breast cancer as initial endocrine-based therapy. ***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 ribociclib 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.*** No comments. ***Do you consider ribociclib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it***	

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		might improve the way that current need is met (is this a 'step change' in the management of the condition)? Ribociclib is a selective Cyclin-dependent kinases (CDK4/6) inhibitor which is a new class of therapy in the management of advanced breast cancer. The aim is to selectively interrupt cell-cycle regulation in cancer cells by interfering with CDK action. Ribociclib is a selective CDK4/6 inhibitor with a novel mechanism of action that blocks cell proliferation and cellular DNA synthesis by preventing cell-cycle progression from G1 to S phase by preventing RB phosphorylation The efficacy observed in patients treated with ribociclib, together with its tolerable toxicity profile, represents a step-change in the management of women with metastatic breast cancer. ***Do you consider that the use of ribociclib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?*** No comments. Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits. 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	

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		Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction-	
Additional comments on the draft scope/matrix	Novartis Pharmaceuticals UK Ltd	It should be noted that Pfizer are currently involved in a Technology Appraisal with NICE for palbociclib for treating metastatic hormone receptor-positive, HER2-negative breast cancer (ID915)	Comment noted.

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

None