National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Atezolizumab for untreated, locally advanced or metastatic, triple negative PD-L1-positive breast cancer [ID1522]

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	Roche	The anticipated licence is as follows: "Tecentriq in combination with nab-paclitaxel is indicated for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) whose tumours have PD-L1 expression ≥1% and have not received prior chemotherapy for metastatic disease" We recommend the remit is updated to reflect this.	Thank you for your comment. The remit, the title and definition of the scope population has been updated accordingly.
	Breast Cancer Now	Yes.	Thank you for your comment. The remit has been updated based on the anticipated marketing authorisation.
Timing Issues	Roche	The prognosis for women with mTNBC is worse than for patients with HER2-positive or hormone receptor-positive disease. mTNBC is incurable and	Thank you for your comments. The dates of

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		patients usually experience a short relapse time to palliative chemotherapy and poor long-term survival. There is no targeted therapy available for patients with mTNBC and chemotherapy is the standard of care. Patients need new treatments that can improve their clinical outcomes and quality of life. Atezolizumab in combination with nab-paclitaxel has demonstrated considerable improvement in outcomes versus chemotherapy in the IMpassion130 trial, with Marketing Authorisation anticipated in [redacted]. In addition, atezolizumab has been designated PIM status, and [redacted], therefore, it is critical this appraisal continues without delay to prevent patients missing an opportunity of treatment with a significant advance over current standard of care.	the expected marketing authorisation were taken into account when the topic was planned into the work programme. No action needed
	Breast Cancer Now	Triple negative breast cancer is associated with lower survival rates than other types of breast cancer but innovative and clinically-effective therapies remain an area of significant unmet need for this patient group. Triple negative breast cancer is typically difficult to treat due to the absence of oestrogen, progesterone and human epidermal growth factor receptors and as a result there are currently limited treatment options available to patients beyond standard chemotherapy. It would therefore be helpful if this appraisal could be progressed quickly as it is essential that this patient group have access to the best available treatments which can offer clinical benefit.	Thank you for your comments. The dates of the expected marketing authorisation were taken into account when the topic was planned into the work programme. No action needed

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Roche	Paragraph two states “The 5-year survival rate for people with metastatic breast cancer in England is 15%”. However, survival rates for mTNBC are considerably lower; As of 2014, the five-year overall survival (OS) rate for mTNBC was estimated at 9% (based on the most recent estimates from the Surveillance, Epidemiology, and End Results [SEER] database). As such, the scope should highlight more clearly the anticipated survival rate for this subgroup of breast cancer.	Thank you for your comment. The scope includes only a brief description of the disease area. Please include the survival information from the US population in your submission. No action needed.
	Breast Cancer Now	Yes the background information appears correct.	Thank you for your comment. No action needed.
The technology/ intervention	Roche	Yes, the description of the technology is accurate	Thank you for your comment. No action needed.
	Breast Cancer Now	Yes to the best of our knowledge.	Thank you for your comment. No action needed.
Population	Roche	The anticipated licence is as follows: “Tecentriq in combination with nab-paclitaxel is indicated for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) whose tumours have PD-L1 expression ≥1% and have not received prior chemotherapy for metastatic disease” As such, the population should be amended to capture the appropriate PD-L1	Thank you for your comment. The remit, the title and definition of the scope population has been updated accordingly.

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		status.	
	Breast Cancer Now	The population appears to be defined appropriately. NICE may want to consider those with a PD-L1 biomarker separately.	Thank you for your comment. The definition of the scope population has been updated based on the anticipated marketing authorisation.
Comparators	Roche	The comparators listed on the draft scope are representative of the NICE treatment pathway for metastatic TNBC. However there are important differences in clinical practice that should be highlighted: • The majority of patients won't be suitable for anthracylines as ~80-90% of patients are early BC relapses, thus will likely have received anthracyclines in the (neo)adjuvant setting. Only ~10-20% of patients present with mTNBC *de novo* and could be initiated on anthracylines. • Based on clinical expert opinion gathered by Roche and supported by market research, paclitaxel is the preferred treatment option for 1L metastatic TNBC due to the more manageable toxicity profile associated with the weekly dosing regimen. As such, paclitaxel should be added to the scope, or should replace docetaxel.	Thank you for your comment. Paclitaxel was added to the list of comparators.
	Breast Cancer Now	Yes.	Thank you for your comment. Paclitaxel was added to the list of comparators.

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Outcomes	Roche	Yes, the listed outcomes capture the most important health related benefits and harms.	Thank you for your comment. No action needed.
	Breast Cancer Now	Yes.	Thank you for your comment. No action needed.
Economic analysis	Roche	Atezolizumab in combination with nab-paclitaxel has demonstrated considerable benefit over chemotherapy, thus a cost effectiveness analysis is the most appropriate economic analysis. This will be expressed in terms of incremental cost per quality-adjusted life year. The time horizon should be sufficient to capture all health related benefits and costs of treatment: a lifetime horizon that captures the full expected overall survival of patients is the appropriate time horizon.	Thank you for your comment. No action needed.
	Breast Cancer Now	No comment.	-
Equality and Diversity	Roche	No equality issues have been identified.	Thank you for your comment. No action needed.
	Breast Cancer Now	The scope does not appear to promote discrimination.	Thank you for your comment. No action needed.
Other considerations	Roche	As the anticipated licence covers patients who are PD-L1 positive, it will not be necessary to explore the subgroup of patients without a PD-L1 biomarker.	Thank you for your comment. Subgroups were removed from the scope.
Innovation	Roche	Promising Innovative Medicine (PIM) Designation was issued in November 2018 for atezolizumab in combination with nab-paclitaxel for the treatment of	Thank you for your

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		adult patients with unresectable locally advanced or metastatic triple-negative breast cancer, and [redacted]. The PIM status indicates that atezolizumab represents a significant advance in a disease with a high unmet clinical need, [redacted] In the phase III study, IMpassion130, atezolizumab in combination with nab-paclitaxel has demonstrated superior efficacy versus nab-paclitaxel in combination with placebo. This includes: • A statistically significant improvement in progression free survival in the PD-L1-positive population (median 7.5 months vs. 5.5 months [HR:0.62; CI: 0.49-0.78; p<0.001]) • A clinically meaningful improvement in overall survival in the PD-L1-population (median 25.0 months vs. 15.5 months [HR: 0.62; CI: 0.45-0.86; p-value not tested due to statistical hierarchy testing in clinical trial]) IMpassion130 represents the first improvement in survival in mTNBC in 20 years, thus is considered a significant step change for the management of this condition.	comments. Innovation will be considered in detail by the committee during the appraisal. No action needed.
	Breast Cancer Now	We consider atezolizumab to be an innovative and novel immunotherapy for the treatment of metastatic triple negative breast cancer. It could expand first line treatment options beyond chemotherapy and fill the gap in treatment options available for this population group.	Thank you for your comments. Innovation will be considered in detail by the committee during the appraisal. No action needed.

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Questions for consultation	Roche	• Have all relevant comparators for atezolizumab been included in the scope? Please see comment on comparators above. One comparator is missing: paclitaxel. Which treatments are considered to be established clinical practice in the NHS for untreated locally advanced or metastatic, triple negative breast cancer? • What is the standard chemotherapy for untreated advanced triple negative breast cancer? Please see comment on comparators above. Based on market research and clinical expert opinion, paclitaxel is deemed the preferred treatment regimen. • Is a PD-L1 testing routinely used in NHS for untreated locally advanced or metastatic, triple negative breast cancer? PD-L1 testing is not yet routinely used in the NHS for breast cancer. • Are the outcomes listed appropriate? Yes. Please see comments on outcomes above. • Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom atezolizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? Atezolizumab is anticipated to receive a licence for patients with PD-L1 positive disease. As such, the subgroup of patients without this biomarker would not be eligible for treatment and their inclusion is not appropriate. No further subgroups have been identified. • Where do you consider atezolizumab will fit into the existing NICE pathway, Advanced breast cancer? Atezolizumab in combination with nab-paclitaxel will be used first line in	Thank you for your comments. The list of comparators, the scope population, the definition of subgroups and the remit have been updated.

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		mTNBC patients whose tumours have PD-L1 expression ≥1% and have not received prior chemotherapy for metastatic disease. • 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 atezolizumab 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. No comment • Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts. Clinical trial results from Phase III IMpassion130 trial. • Do you consider atezolizumab 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)? Yes, atezolizumab has demonstrated considerable improvement in outcomes in this setting, thus is considered a step change in the management of this condition. As detailed above, PIM designation has been given for	

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		atezolizumab in combination with nab-paclitaxel for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC). Following the PIM designation, [redacted] • Do you consider that the use of atezolizumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? No comment • Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits. Phase III randomised clinical trial: IMpassion130 providing robust progression free survival and overall survival data. • 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. PD-L1 testing will be required to identify patients with mTNBC eligible for treatment. • 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). This process is appropriate.	
	Breast Cancer	Under "related NICE recommendations and NICE pathways", it states that	Thank you for your

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	Now	Tumour profiling tests to guide adjuvant chemotherapy decisions in people with breast cancer is relevant. However, this guidance does not look at patients with triple negative breast cancer, it is instead for a certain group of breast cancer patients with hormone receptor positive breast cancer. Are the subgroups suggested in 'other considerations' appropriate? Yes we consider people with a PD-L1 biomarker to be an appropriate subgroup as the trial looked at this particular group, and published the separate PFS results.	comments. **'**Tumour profiling tests to guide adjuvant chemotherapy decisions in people with breast cancer' has been removed from the scope. The definition of the scope population has been updated based on the anticipated marketing authorisation.

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

None.