National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Atezolizumab with chemotherapy for neoadjuvant treatment of resectable early or locally advanced invasive triple-negative breast cancer [ID1574]

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 Products Ltd	The anticipated license is as follows: Tecentriq, in combination with nab-paclitaxel and anthracycline-based chemotherapy, is indicated for the neoadjuvant treatment of [redacted] We recommend that the remit is updated to reflect this. Furthermore, we also recommend that the technology appraisal and scope titles are updated to reflect this.	Thank you for confirming the anticipated licence wording. No changes to the remit or the scope title are needed.
	Breast Cancer Now	Yes, the wording is appropriate.	Thank you for your comment.
Timing Issues	Roche Products	The prognosis for women with triple negative breast cancer (TNBC) is worse	Thank you for your

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	Ltd	than for patients with HER2- positive or hormone receptor-positive disease. Patients with high-risk early TNBC are associated with early recurrence and high mortality, despite the best standard-of-care chemotherapy treatment available. Neoadjuvant therapy is the recommended treatment approach to reduce the risk of relapse for these patients. However, there is no targeted therapy available in this setting. Patients need new treatments that can improve their long-term outcomes. Atezolizumab in combination with nab-paclitaxel and anthracycline-based chemotherapy has demonstrated a statistically significant and clinically meaningful improvement in its primary outcome (Pathologic Complete Response) versus nab-paclitaxel and anthracycline-based chemotherapy in the IMpassion031 trial. The Marketing Authorisation for this indication is anticipated in [redacted]. We encourage this appraisal to continue in line with the current NICE timelines without delay, to prevent patients missing an opportunity of treatment with a significant advance over the current standard of care.	comment. This topic has been scheduled into the work programme.
	Breast Cancer Now	Clinical trial data has shown this treatment option could be effective in improving pathological complete response in this group of patients. Treatment options for triple negative breast cancer remain limited, and triple negative breast cancer tends to be more aggressive and is associated with a poorer prognosis than other types of breast cancer. New treatments which can improve pathological complete response rate and may potentially improve breast conservation in people with triple negative is very welcome. We now	Thank you for your comment. This topic has been scheduled into the work programme.

Section	Consultee/ Commentator	Comments [sic]	Action
		hope the appraisal of this treatment can be progressed in a timely manner.	

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Roche Products Ltd	N/A	Thank you.
	Breast Cancer Now	The information is accurate.	Thank you for your comment.
The technology/ intervention	Roche Products Ltd	We recommend amending the description of the technology, so that it is aligned with the anticipated marketing authorisation statement, to: "Neoadjuvant atezolizumab in combination with nab-paclitaxel and anthracycline-based chemotherapy"	Thank you for your comment. The technology section provides an overview of the technology and this detail is not required. No changes to the scope are needed.
	Breast Cancer Now	Yes to the best of our knowledge.	Thank you for your comment.
Population	Roche Products Ltd	The evidence submission will address the following population: "Atezolizumab in combination with nab-paclitaxel and anthracycline-based chemotherapy for neoadjuvant treatment of [redacted]	Thank you for confirming the anticipated licence.

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		The reason for this differing from the NICE pre-invitation scope is that this wording directly reflects the anticipated license.	
	Breast Cancer Now	Yes to the best of our knowledge.	Thank you for your comment.
Comparators	Roche Products Ltd	The current neoadjuvant standard of care in the NHS for patients with locally advanced or early TNBC, and therefore potential comparator for this appraisal is: • Anthracycline-containing neoadjuvant chemotherapy regimen, with taxane and/or platinum.	Thank you for your comment. The comparator in this scope is standard neoadjuvant chemotherapy without atezolizumab, which includes the example provided. No changes to the scope are needed.
	Breast Cancer Now	The current standard of treatment for this group of patients on the NHS is chemotherapy. As recommended by NICE, people with triple negative breast cancer may receive a neoadjuvant chemotherapy regimen that contains both a platinum and an anthracycline. Standard chemotherapy may include combined anthracycline (epirubicin or doxorubicin) and cyclosphosphamide plus a taxane based regime (docetaxel or paclitaxel).	Thank you for your comment. The comparator in this scope is standard neoadjuvant chemotherapy without atezolizumab, which includes the example provided. No changes to the scope are needed.
Outcomes	Roche Products	The primary outcome measure that should be considered for this appraisal,	Thank you for your

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	Ltd	which is a common patient-relevant endpoint for breast cancer, is: • Pathologic Complete Response (pCR). Impassion031 included but was not powered for other outcomes including: • Event-Free Survival (EFS) • Disease Free Survival (DFS) • Overall Survival (OS) • EORTC QLQ-C30 • Adverse Events (AEs) of treatment • Serum concentration • Percentage of patients with Anti-Drug Antibodies (ADAs) to atezolizumab	comment. Pathologic Complete Response is covered by the outcome of 'response rate' listed in the scope. The list of outcomes included in the scope is not exhaustive. No changes to the scope are needed.
	Breast Cancer Now	Yes	Thank you for your comment.
Economic analysis	Roche Products Ltd	Atezolizumab in combination with nab-paclitaxel and anthracycline based chemotherapy has demonstrated statistically significant and clinical meaningful benefit over nab-paclitaxel and anthracycline-based chemotherapy in IMpassion031, thus a cost-effectiveness analysis is indeed the most appropriate economic analysis. This will be expressed in terms of incremental cost per quality-adjusted life years (Cost per QALYs). 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 for this appraisal.	Thank you for your comment.
	Breast Cancer Now	No comment	Thank you for your comment.

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Equality and Diversity	Roche Products Ltd	No equality issues have been identified.	Thank you for your comment.
	Breast Cancer Now	The scope does not appear to promote discrimination.	Thank you for your comment.
Innovation	Roche Products Ltd	IMpassion031 represents a significant improvement versus the current standard of care in the neoadjuvant treatment space in early TNBC, thus is considered a significant step change for the management of this condition. Atezolizumab with its innovative mechanism of action, selectively targeting programmed death ligand 1 (PD-L1), was the first cancer immunotherapy approved for use in triple negative breast cancer (TNBC). Expanding on the impact of atezolizumab in metastatic TNBC, IMpassion031 represents a significant improvement versus the current standard of care in the neoadjuvant treatment of early TNBC. As a result, atezolizumab provides another step change for the management of TNBC. The phase III IMpassion031 clinical trial successfully met its primary endpoint, demonstrating that atezolizumab in combination with nab-paclitaxel and anthracycline-based chemotherapy, achieved a statistically significant and clinically meaningful increase in pathological complete response (pCR) versus placebo with nab-paclitaxel and anthracycline-based chemotherapy in the intention-to-treat (ITT) population. Meaning that benefit was observed regardless of PD-L1 status and across all clinical subgroups. This includes [i]:	Thank you for your comment. The appraisal committee will consider the innovative nature of this technology when making its recommendations. No changes to the scope are needed.

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		• Documented pathological complete response in 95 (58%, 95% CI 50–65) patients in the atezolizumab plus chemotherapy group versus 69 (41%, 34–49) patients in the placebo plus chemotherapy group (**rate difference 17%,** 95% CI 6–27; one-sided p=0·0044 [significance boundary 0·0184]). • In the PD-L1-positive population: Documented pathological complete response in 53 (69%, 95% CI 57–79) of 77 patients in the atezolizumab plus chemotherapy group versus 37 (49%, 38–61) of 75 patients in the placebo plus chemotherapy group **(rate difference 20%**, 95% CI 4–35; one-sided p=0·021 [significance boundary 0·0184])	
	Breast Cancer Now	We consider atezolizumab to be an innovative technology for the treatment of triple negative breast cancer. It could provide an important addition to neoadjuvant chemotherapy for this patient group. There are currently no other immunotherapies available on NHS to treat early triple negative breast cancer.	Thank you for your comment. The appraisal committee will consider the innovative nature of this technology when making its recommendations. No changes to the scope are needed.
Questions for consultation	Roche Products Ltd	**Is the population defined in the scope appropriate?** Please see relevant comment in section 2 above. **What proportion of people with early or locally advanced invasive triple-negative breast cancer are given a neoadjuvant chemotherapy regimen that contains both a platinum agent and an anthracycline?** The proportion of patients treated with anthracycline in combination with a	Thank you for your comment. No changes to the scope are needed.

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		platinum based chemotherapy varies considerably across all trusts. **Are the outcomes listed appropriate?** Pathological complete response (pCR), the primary outcome of IMpassion031 is the most commonly used endpoint in neoadjuvant trials and has been associated with improved prognosis, and survival outcomes in breast cancer. **Are there any subgroups of people in whom atezolizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?** The phase III clinical trial IMpassion031 has demonstrated superior efficacy across the entire Intention To Treat (ITT) population. The ITT population of IMpassion031 is also in line with the anticipated marketing authorisation and is expected to be examined in its totality. **Where do you consider atezolizumab will fit into the existing NICE pathway, Early and locally advanced breast cancer?** Atezolizumab in combination with nab-paclitaxel and anthracycline-based chemotherapy will fit as the neoadjuvant treatment of choice [redacted] **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**	

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		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.** N/A **Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.** N/A **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)?** Please see relevant comment is section 2 above. **Do you consider that the use of atezolizumab can result in any potential significant and substantial health-related benefits that are unlikely to be**	

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		included in the QALY calculation? N/A **Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.** N/A **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.** N/A	

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

None.