National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Pembrolizumab in combination with chemotherapy for neoadjuvant treatment of locally advanced triple 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	Merck, Sharp and Dohme (MSD)	No comment	No action required
Timing Issues	MSD	Patients with early triple negative breast cancer (TNBC) may receive neoadjuvant chemotherapy followed by surgical resection of the tumour. However, no advances in neoadjuvant or adjuvant chemotherapy have been made recently for these patients and long-term survival outcomes with the current treatment options remain poor. We anticipate the proposed appraisal should be scheduled as soon as possible to enable NICE to issue final guidance soon after regulatory approval. The information on anticipated regulatory timelines presented in PharmaScan accurately reflects current expectations.	Comment noted. No action required

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	MSD	No comment.	No action required
The technology/ intervention	MSD	The draft scope wording does not accurately reflect the intervention. MSD suggests it should read “a single regimen of pembrolizumab plus chemotherapy for neo-adjuvant treatment followed by monotherapy pembrolizumab for adjuvant treatment”. KEYNOTE-522 was designed with pembrolizumab as a single regimen, being given in the neoadjuvant and adjuvant phases of treatment.	Thank you for your comment. The technology section of the scope has been updated.
Population	MSD	MSD suggests the population should be [redacted]” to reflect the anticipated licence wording.	Thank you for your comment. As the information on the population provided has been marked commercial in confidence, this change cannot be made. No change to scope made.
Comparators	MSD	The chemotherapy regimens used in the neoadjuvant phase in KEYNOTE-522 were carboplatin + paclitaxel (cycles 1-4) followed by doxorubicin/epirubicin + cyclophosamide (cycle 5-8) with pembrolizumab or placebo during cycles 1 to 8 (see Appendix A for trial design). Based on clinical guidelines, MSD believes the neoadjuvant phase of KEYNOTE-522 is reflective of NHS practice and therefore the placebo arm is suitable to be used as the comparator.	A list of chemotherapy drugs commonly used in the neoadjuvant treatment of triple negative breast cancer in clinical practice has been included in the

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		The treatment in the adjuvant phase of KEYNOTE-522 is monotherapy is with placebo for 9 cycles. Based on current UK guidelines and clinical practice, the adjuvant part of the study is also reflective of the UK clinical practice.	background section of the scope
Outcomes	MSD	MSD suggests that pathological complete response (pCR) and event free survival (EFS) should be added. The primary outcomes in KEYNOTE-522 are pCR defined as ypT0/Tis ypN0 and EFS. Overall survival is a secondary outcome and the database lock for final analysis is anticipated to occur in [redacted]. MSD suggests that disease free survival, surgical outcomes and response rate should be removed as these are not primary or secondary outcomes in KEYNOTE-522. MSD agrees with the inclusion of adverse effects of treatment and Health-related quality of life.	Thank you for your suggestions. The outcomes suggested have been included in the scope.
Economic analysis	MSD	No additional comments.	Comment noted.
	BCN	No comment.	Comment noted.
	MSD	No additional comments.	Comment noted.

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Equality and Diversity	BCN	The scope does not appear to promote discrimination.	Comment noted.
Other considerations	MSD	No additional comments	Comment noted.
Innovation	MSD	MSD considers pembrolizumab to be innovative in its potential to make a significant and substantial positive impact on health-related benefits. [redacted] has the potential to improve outcomes for patients with triple negative breast cancer. Pembrolizumab would be the first licenced anti-PD-1 pathway targeting agent to be approved for neoadjuvant and adjuvant treatment of triple negative breast cancer.	Comment noted. Innovation will be considered by the appraisal committee when formulating its recommendations. The consultees and commentators will have an opportunity to provide evidence on the innovative nature of the product in their submissions.
Questions for consultation	MSD	**Have all relevant comparators for pembrolizumab been included in the scope?** See comment above in comparator section **Which treatments are considered to be established clinical practice in the NHS for neoadjuvant and adjuvant treatment of locally-advanced, non-metastatic triple-negative breast cancer?** See comment above in comparator section	Thank you for your responses. No changes to the scope needed.

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		What neoadjuvant and adjuvant chemotherapies are given when treating locally, non-metastatic triple negative breast cancer? See comment above **Are the outcomes listed appropriate?** See comment above in outcomes section **Are there any subgroups of people in whom pembrolizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?** None. **Where do you consider pembrolizumab will fit into the existing NICE pathway?** In line with the anticipated marketing authorisation, pembrolizumab in combination with chemotherapy followed by pembrolizumab monotherapy would be used as a treatment option for those with [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 remit and scope:**	

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		• could exclude from full consideration any people protected by the equality **legislation who fall within the patient population for which pembrolizumab 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 **Do you consider pembrolizumab 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 - see comment above in innovation section. **Do you consider that the use of pembrolizumab can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?** All potential significant and substantial health-related benefits are captured in the QALY calculation	

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		Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits Not applicable **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.** MSD does not anticipate any barrier to adoption of this technology. **NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments** The STA process is appropriate for this technology	

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

None.