National Institute for Health and Care Excellence

Health Technology Evaluation

Cemiplimab for treating recurrent or metastatic cervical cancer that has progressed on or after platinum-based chemotherapy (review of TA901)
Response to stakeholder organisation comments on the draft remit and draft scope

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 and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Regeneron	Evaluation and proposed route are appropriate.	Thank you for your comment. No action needed.
Wording	Regeneron	'Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider? If not, please suggest alternative wording.' – Yes.	Thank you for your comment. No action needed.
Timing issues	Regeneron	This is an area of high unmet medical need in a small population of often young patients who have a very poor prognosis. As reported in the draft scope, there is currently no second line standard of care option for patients advanced cervical cancer. Chemotherapies used currently are associated with poor response rates and high rates of toxicity.1	Thank you for your comment. No action needed.

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		Cemiplimab offers a significant survival gain and clinically meaningful differences in patients' quality of life compared with current treatment.2,3 There is therefore an urgent need to make it available to patients on the NHS in England as soon as possible.	

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Regeneron	1. Although a small minority of patients may opt to have no further active treatment after progressing on or after first-line treatment, Regeneron do not consider best supportive care to be a routine second line option (see below). 2. On p.2, please change the name of the submitting company from Sanofi to Regeneron, and change the brand name from Libtavo to Libtayo.	Thank you for your comment. Factual inaccuracies have been updated in the updated scope. NICE aims to keep the comparator list as inclusive as possible even if only a small proportion of population is expected to have a treatment therefore, NICE considers best-supportive care an appropriate comparator.
Population	Regeneron	'Is the population defined appropriately?' – Yes.	Thank you for your comment.

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			No action needed.
Subgroups	Regeneron	**Within its marketing authorisation, there is no subgroup in which cemiplimab is expected to be either more or less clinically or cost-effective than the overall population.** The draft scope suggests two subgroups for consideration. Regeneron does not consider these subgroups to be appropriate, because the trial data show that they are not treatment-effect modifiers. **1. Histology (squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma).** The EMPOWER-Cervical 1 trial was stratified by histological subgroup (squamous vs adenocarcinoma [including adenosquamous carcinoma], and results were reported both in the separate histology groups and the overall study population. Most patients (77.8%) had squamous histology. Median overall survival in the cemiplimab arm (final analysis) was very similar between the overall population (n=304; 11.7 months; HR 0.67, 95 % confidence interval [CI] 0.56–0.80), the squamous histology population (n=239; 10.9 months; HR 0.70, 95 % CI 0.57–0.86), and the adenocarcinoma/adenosquamous population (n=66; 13.5 months; HR 0.55, 95 % CI 0.37–0.82 [exploratory analysis]).2 Histology was therefore not a treatment-effect modifier, and this is reflected in the marketing authorisation, which does not specify histology.2	Thank you for your comment. These subgroups have been removed from the scope.

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		2. Prior treatment (bevacizumab, paclitaxel or people with a clinically documented reason why not administered). Previous bevacizumab exposure (yes/no) was also a stratification factor in the trial, and approximately 50% of patients in each treatment arm had prior bevacizumab. Patients experienced an overall survival benefit with cemiplimab versus chemotherapy regardless of prior bevacizumab exposure (HR [redacted] [95% CI [redacted]] with and HR [redacted] without), indicating no statistically significant difference between the two groups.	
Comparators	Regeneron	Single-agent chemotherapy is considered the only relevant comparator. Best supportive care: Regeneron do not consider best supportive care4 to be a relevant comparator after progression on platinum-based chemotherapy, because a range of second-line chemotherapy options are available, and the majority of patients will receive active 2L treatment. According to the four clinical experts, who were interviewed by Regeneron to assess current clinical practice in England and Wales, the majority of patients receive either chemotherapy or are enlisted in clinical trials. The minority of patients who are not suitable for active 2L treatment with existing chemotherapy options are also not anticipated to be eligible for cemiplimab. Tisotumab vedotin monotherapy: Regeneron do not consider tisotumab vedotin to be a relevant comparator as its use cannot be considered to be established clinical practice: it is not currently in routine use in NHS clinical practice,	NICE aims to keep the comparator list as inclusive as possible even if only a small proportion of population is expected to have a treatment therefore, NICE considers best-supportive care an appropriate comparator. For the same reason of inclusivity, tisotumab vedotin has been maintained as an appropriate comparator. NICE recognises that including tisotumab vedotin in the appraisal will be dependent on

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		it does not currently have a positive recommendation for use by NICE, NICE guidance for tisotumab vedotin is not scheduled to be published until 25th June 2026,5 which is >6 months after the scheduled submission date for cemiplimab, and >1 month after the scheduled appraisal committee meeting for cemiplimab. Even if NICE makes a positive recommendation for tisotumab vedotin, it cannot reasonably be considered to have become established clinical practice within the timescale of the appraisal of cemiplimab.	the schedule and result of NICE evaluation.
Outcomes	Regeneron	Yes, the outcomes listed are appropriate. However, some of the benefits of cemiplimab are not fully captured by the QALY calculation (see below).	Thank you for your comment. No action needed.
Equality	Regeneron	It should be noted that decision-making in relation to cervical cancer treatments disproportionately affects people with high levels of socioeconomic deprivation: Cancer Research UK states that: “Cervical cancer incidence rates in England in females are 65% higher in the most deprived quintile compared with the least (2013-2017).” 6 While this should be taken into consideration by the Committee, Regeneron do not consider that any changes to the draft remit and scope are needed in relation to this issue.	Thank you for your comment. The committee will consider evidence on the equality issues raised during the course of the appraisal. No action needed.
Other considerations	Regeneron	None.	

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Questions for consultation	Regeneron	Current treatment pathway The established first-line treatment for metastatic or recurrent cervical cancer (r/m CC) for patients who are eligible for pembrolizumab is pembrolizumab + chemotherapy +/- bevacizumab.4 Patients who are not eligible for pembrolizumab receive platinum-based chemotherapy, typically platinum paclitaxel doublet +/- bevacizumab.7 In second line (2L) after platinum-based chemotherapy, patients currently have no option other than further chemotherapy. There is no standard recommended regimen.7 Pembrolizumab is not generally used in 2L, because eligible patients will have received it in 1L. Few patients currently receive 3L treatment. The options are further chemotherapy, or a clinical trial. Position of cemiplimab in pathway Cemiplimab is proposed as a more effective and better-tolerated alternative to further chemotherapy in patients with r/m CC and disease progression on or after platinum-based chemotherapy, in line with its licensed indication. In line with the pivotal study population and clinical guidelines,8 it is anticipated that cemiplimab will be used in patients who have not received prior immunotherapy.	Thank you for your comments no action needed.

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		Population relative to tisotumab vedotin The use of tisotumab vedotin after platinum-based chemotherapy would involve two consecutive lines of chemotherapy, which may have negative implications for tolerability and quality of life compared with use of an immunotherapy in second line. Consequently, the proportion of patients suitable for tisotumab vedotin in the second-line setting would potentially be lower than the proportion suitable for cemiplimab. If tisotumab vedotin entered routine clinical practice, then tisotumab vedotin and cemiplimab might be offered to similar populations, as their licensed indications overlap. However, cemiplimab provides a chemotherapy-free immunotherapy option for those patients who have not received first-line immunotherapy. Tisotumab vedotin is a chemotherapy rather than an immunotherapy, and as such could be offered to patients who have received prior immunotherapy. We therefore anticipate that, in practice, clinicians and patients may use cemiplimab and tisotumab vedotin in different populations. Notwithstanding the theoretical overlap in their licensed indications, tisotumab vedotin should not be considered a relevant comparator to cemiplimab, as its use will not be established clinical practice within the timescales of the appraisal of cemiplimab, as explained above. Prescribing setting	

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		Cemiplimab will be prescribed in secondary care with routine follow-up in secondary care. This setting is the same as that of the comparator. Managed access Cemiplimab is not considered a candidate for managed access, because the survival data from the pivotal trial are highly mature. At the time of the final analysis (median follow-up 47.3 months), 78% and 84% of patients in the cemiplimab and chemotherapy arms, respectively, had died.2 Consequently, the level of uncertainty around survival is lower than in most oncology appraisals, and would not be meaningfully reduced by further data collection in managed access. Benefits not captured by the QALY Cervical cancer affects a younger age group than many other cancers, with incidence rates in England peaking at age 30-34 years.6 People with r/m CC are often young, and many have dependent children or other caring responsibilities. The Patient and Clinician Engagement (PACE) statement from the SMC appraisal of cemiplimab in this indication9 notes that “the ability to continue caring for their families [both children and older relatives] is of the upmost importance to this patient group, and minimising time in hospital whilst providing meaningful clinical benefit cannot be underestimated.” The pivotal trial did not measure quality of life impact for families and caregivers arising from the benefits that patients experienced with cemiplimab, and this is therefore not captured by the QALY. Additionally, the 3-week dosing interval of cemiplimab means receiving treatment is less disruptive than	

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		weekly paclitaxel infusions, which are a common 2L regimen in England. This benefit to patients and families is also not captured by the QALY.	

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

None