National Institute for Health and Care Excellence

Health Technology Evaluation

Tisotumab vedotin for treating recurrent or metastatic cervical cancer that has progressed on or after systemic treatment [ID3753] 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	British Gynaecological Cancer Society	It is important to evaluate this topic as management of recurrent cervical cancer is challenging, with no standard therapy arms following chemotherapy.	Thank you for your comment. This topic will be evaluated as a single technology appraisal.
Wording	Genmab A/S	The current NICE Draft remit.evaluation objective reads: To appraise the clinical and cost effectiveness of tisotumab vedotin within its marketing authorisation for treating recurrent or metastatic cervical cancer after chemotherapy. This should be updated to align with the proposed MHRA marketing authorisation:	Thank you for your comment. The remit has been updated in line with the proposed UK marketing authorisation.

Section	Stakeholder	Comments [sic]	Action
		"To appraise the clinical and cost effectiveness of tisotumab vedotin as monotherapy for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after systemic therapy"	
	British Gynaecological Cancer Society	Yes	Thank you for your comment. The remit has been updated in line with the proposed UK marketing authorisation.
Timing Issues	Genmab A/S	The provision of an innovative antibody-drug conjugate which constitutes a step change in the treatment of r/mCC. Tisotumab vedotin will provide patients and clinicians with an alternative and effective therapy for a patient population with significantly poor treatment outcomes and high unmet need for effective alternatives to standard chemotherapy.	Thank you for your comment. This topic has been scheduled into NICE's work programme. For further details please see the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ta10620
	British Gynaecological Cancer Society	Urgent – there is no alternative option currently available. The randomised trial data showing benefit with this treatment compared to standard of care has been available for > 2 years, and this is now standard of care in USA (NCCN guidelines).	Thank you for your comment. This topic has been scheduled into NICE's work programme. For further details please see the NICE website: https://www.nice.org.uk/

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			guidance/indevelopment/gid-ta10620

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Genmab A/S	The background information does not currently reflect the high burden of disease of relapsed or metastatic cervical cancer. Genmab recommend the inclusion of the following wording: *"Compared with early-stage cervical cancer survival is significantly lower among women with relapsed and metastatic disease (1-7)."* Regarding the technology Genmab recommends that the wording is updated to reflect the expected UK MHRA marketing authorisation as follows (aligned to EMA marketing authorisation statement (28th March 2025): *"Tisotumab vedotin (Tivdak, Genmab) does not currently have a marketing authorisation in the UK for treating recurrent or metastatic cervical cancer. It has been studied in clinical trials in people with recurrent or metastatic cervical cancer with disease progression on or after systemic therapy."* **References**: 1. Cromwell I, Ferreira Z, Smith L, van der Hoek K, Ogilvie G, Coldman A, et al. Cost and resource utilization in cervical cancer management: a real-world retrospective cost analysis. Curr Oncol. 2016;23(Suppl 1):S14-22.	Thank you for your comment. The background section of the scope has been updated to include information about survival in recurrent or metastatic cervical cancer. The technology section of the scope has been updated in line with the anticipated UK marketing authorisation.

Section	Consultee/ Commentator	Comments [sic]	Action
		2. Yoshida K, Kajiyama H, Utsumi F, Niimi K, Sakata J, Suzuki S, et al. A post-recurrence survival-predicting indicator for cervical cancer from the analysis of 165 patients who developed recurrence. Mol Clin Oncol. 2018;8(2):281-5. 3. Usami T, Takahashi A, Matoda M, Okamoto S, Kondo E, Kanao H, et al. Review of Treatment and Prognosis of Stage IVB Cervical Carcinoma. Int J Gynecol Cancer. 2016;26(7):1239-45. 4. Inocencio T, Wu N, Ge W, Gleeson M, Monk B. Healthcare costs among real-world patients with recurrent or metastatic cervical cancer (r/mCC) receiving second-line (2L) treatment. Value in Health. 2022;25(7). 5. Alholm Z, Monk JB, Ting J, Pulgar S, Boyd M, Sudharshan L, et al. Patient characteristics, treatment patterns, and clinical outcomes among patients with previously treated recurrent or metastatic cervical cancer: A community oncology-based analysis. Gynecologic Oncology. 2021;161(2):422-8. 6. Gokhale M, Yu R, Monberg M, Tekin C, Chen L, DeClue R, et al. Patient profiles, treatment patterns, and outcomes among persistent, recurrent, or metastatic cervical cancer patients under routine care in the United States. Cancer Treat Res Commun. 2023;36. 7. 7. Khachatryan A, Doobaree I, Banon T. HSD26 Real-World Patterns of Care and Outcomes Among Advanced Cervical Cancer Patients in England: Retrospective Analysis of the NCRAS Datasets, 2012-2019. Value in Health. 2022;25(12).	
	British Gynaecological Cancer Society	The background considers first line therapy options, but does not discuss second line options (or the lack of..) where this technology fits.	Thank you for your comment. The background of the scope has been amended to discuss second line options for

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			recurrent or metastatic cervical cancer.
Population	Genmab A/S	As previously stated, the scope population should align with EU marketing authorisation and the expected UK marketing authorisation as follows: *"Tivdak as monotherapy is indicated for the treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after systemic therapy"*	Thank you for your comment. The population has been updated in line with the expected UK marketing authorisation.
	British Gynaecological Cancer Society	Yes	Thank you for your comment. The population has been updated in line with the expected UK marketing authorisation.
Subgroups	Genmab A/S	The innovaTV 301 trial did not stratify patients by PD-L1 expression level, nor was this patient data collected as part of the trial. Therefore, neither planned nor post hoc analysis by PD-L1 expression level will be possible and this should not be considered a separate subgroup. Tisotumab vedotin is not anticipated to significantly differ in its clinical or cost effectiveness in any other subgroup within the proposed population.	Thank you for your comment. The PD-L1 subgroup has been removed.
	British Gynaecological Cancer Society	Unclear why PDL-1 status is a subgroup. It might be that prior IO is relevant, since the alternative second line option for women who have not had prior immunotherapy (irrespective of PDL1 status) is cemiplimab (not currently available in England / Wales but available in Scotland and is EMA/FDA approved in this setting).	Thank you for your comment. The PD-L1 subgroup has been removed.

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Comparators	Genmab A/S	The comparators in the draft scope are not relevant to the decision problem as they relate to an earlier line of therapy. The decision problem will focus on the second line or later relapsed or metastatic cervical cancer patient population (i.e., those who had progressed during or after systemic chemotherapy doublet or platinum-based therapy with or without bevacizumab). The comparator used in this population in clinical practice is single-agent chemotherapy, including: • irinotecan • vinorelbine • docetaxel • gemcitabine • topotecan	Thank you for your comment. The comparators have been updated to include single-agent chemotherapy and best supportive care. Cemiplimab is not a relevant comparator as it has not been recommended for use in England and Wales.
	British Gynaecological Cancer Society	No – the comparator should be with standard of care for second line therapy – not with first line (which is chemo+/- pembrolizumab). This is monotherapy chemotherapy with gemcitabine, weekly taxol, topotecan, docorubicin – and has really limited efficacy. The alternative comparator is cemiplimab (as above)	Thank you for your comment. Cemiplimab is not a relevant comparator as it has not been recommended for use in England and Wales. The comparators have been updated to include single agent chemotherapy and best supportive care.

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Outcomes	Genmab A/S	The outcomes listed are considered appropriate to capture the benefits of treatment for these patients.	Thank you for your comment. No changes to the scope required.
	British Gynaecological Cancer Society	Yes	Thank you for your comment. No changes to the scope required.
Equality	Genmab A/S	Genmab does not believe there are equality considerations in the draft remit and scope which require alteration. However, it should be noted that, in England, cervical cancer rates are 65% higher in the most deprived quintile vs the least deprived (8). Cervical cancer screening rates are known to be lower among women in deprived populations (9), and while studies examining HPV vaccine uptake by ethnicity and/or socioeconomic status are scarce, evidence suggests uptake is lower among both more deprived, and non-white ethnic populations (10, 11). These factors demonstrate the current inequalities in both the burden of cervical cancer and access to interventions in England, both of which bear consideration in the evaluation of tisotumab vedotin. To reflect the principles of the 2025 NICE modular update on health inequalities, the appraisal should, therefore: • Consider the variation in clinical and economic impact across deprivation subgroups, • Allow for threshold flexibility where clear inequities exist.	Thank you for your comment. The information on cervical cancer rates in areas of deprivation has been added to the Equality Impact Assessment form issued with the final scope.

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		References: 8. England NHS. Cervical cancer elimination by 2040 – plan for England: NHS England; 2025 [Available from: https://www.england.nhs.uk/long-read/cervical-cancer-elimination-by-2040-plan-for-england/. 9. Falcaro M, Soldan K, Ndlela B, Sasieni P. Effect of the HPV vaccination programme on incidence of cervical cancer and grade 3 cervical intraepithelial neoplasia by socioeconomic deprivation in England: population based observational study. BMJ (Clinical research ed). 2024;385. 10. Fisher H, Evans K, Reynolds R, Yates J, Roderick M, Ferrie J, et al. Secondary analyses to test the impact on inequalities and uptake of the schools-based human papillomavirus (HPV) vaccination programme by stage of implementation of a new consent policy in the south-west of England. BMJ open. 2021;11(7). 11. Pollock KG, Tait B, Tait J, Bielecki K, Kirolos A, Willocks L, et al. Evidence of decreased HPV vaccine acceptance in Polish communities within Scotland. Vaccine. 2019;37(5).	
Other considerations	Genmab A/S	Genmab suggests that the following points, which are not covered in the draft scope, may inform the evaluation of tisotumab vedotin in this indication: - There is currently no defined standard of care for 2nd line+ r/mCC, with re-use of earlier therapy lines being common despite a lack of efficacy. There is a high burden and a high unmet need for innovative therapies at this line (12, 13). - Cervical cancer impacts women in their most productive years. CC has a disproportionate impact on younger women with the majority (59%) of	Thank you for your comment. The background section of the scope has been amended to include information on second line treatment options.

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		patients diagnosed at less than 50 years of age (14), when many are in the workforce and/or raising families. With cervical cancer ranking globally as the 4th most common cause of cancer death (15), its profound impact on families and society due to the premature death of women of relatively young age should be emphasised. **References**: 12. Ando H, Bains S, Tang W, Swallow E. Real-world treatment patterns among metastatic cervical cancer patients in Japan. Ann Oncol. 2022;33(Suppl 6):S476-S7. 13. Musa FB, Brouwer E, Ting J, Schwartz NRM, Surinach A, Bloudek L, et al. Trends in treatment patterns and costs of care among patients with advanced stage cervical cancer. Gynecol Oncol. 2022;164(3):645-50. 14. Yonemori K, Kuboki Y, Hasegawa K, Iwata T, Kato H, Takehara K, et al. Tisotumab vedotin in Japanese patients with recurrent/metastatic cervical cancer: Results from the innovaTV 206 study. Cancer Sci. 2022;113(8):2788-97.	
Questions for consultation	Genmab A/S	1. Where do you consider tisotumab vedotin will fit into the existing care pathway for recurrent or metastatic cervical cancer? The target population will be 2L+ r/m CC defined as: Overall population: adult patients with r/m CC who have progressed during or after systemic chemotherapy doublet or platinum-based therapy 2. Is etoposide used in clinical practice to treat recurrent or metastatic cervical cancer?	Thank you for your comments.

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		Genmab understands that etoposide was used in clinical practice prior to the introduction of pembrolizumab. According to NICE's committee slides for TA885 for pembrolizumab in r/mCC (now superseded by TA939), etoposide was used in the 1st line for r/mCC (alongside topotecan and platinum chemotherapy doublet +/- bevacizumab +/- pembrolizumab) (16). However, whether its usage has changed, or to what extent it is used, is unclear. Furthermore, tisotumab vedotin will target patients progressing after 1L treatment for r/mCC. 3. Setting Tisotumab vedotin will be prescribed in secondary care with routine follow-up in secondary care 4. Would tisotumab vedotin be a candidate for managed access? The primary analysis is complete for innovaTV301. Tisotumab vedotin may be considered for managed access / Cancer Drugs Fund in the UK dependent on the timing/ findings in the appraisal. 5. Do you consider that the use of tisotumab vedotin can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? The QALY is likely to capture health-related benefits associated with tisotumab vedotin monotherapy.	

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		6. Equality considerations As stated in the equality section above, cervical cancer risk is increased among deprived populations. Therefore, tisotumab vedotin has the potential to benefit groups in society with the highest unmet need, and who have previously had challenging engagement with preventative measures (screening and vaccination). The positive impact of reimbursement on these populations therefore should be considered as part of the appraisal.	
	British Gynaecological Cancer Society	TV would fit in as a second / third+ line option for cervical and vaginal cancer (unless new data in combination with IO is available) Etoposide is not used except for neuroendocrine / small cell carcinoma.	Thank you for your comments.
Additional comments on the draft scope	Genmab A/S	Genmab recommend that the title of the scope be updated to align with the expected UK MHRA and confirmed EMA marketing authorisations as follows:	Thank you for your comments. The title of the scope has been updated in line with the expected UK marketing authorisation.
Comments on the provisional stakeholder list	Genmab A/S	Genmab considers the following stakeholder to be missing from the stakeholder list as commentator: - Public Health Wales	Thank you for your comment. Public Health Wales are included as commentators for this topic but are not routinely included on the stakeholder list. No changes required.

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

None