**Report Libtayo®- cemiplimab**

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| **Product &****Mechanism of action** | **Authorized indications****Licensing status** | **Essential therapeutic features** | **NHS impact** |
| **Substance:** cemiplimab**Brand Name:** Libtayo**Originator/licensee:** Regeneron Ireland Designated Activity Company (DAC)**Classification:** NI**ATC code:** L01XC33**Orphan Status:****Eu:** No**Us:** No**Mechanism of action:** cemiplimab is a monoclonal antibody, a type of protein that has been designed to recognise and attach to a receptor (target) called PD-1 found on certain cells of the immune system called T cells. Cancer cells can make proteins (PD-L1 and PD-L2) that attach to this receptor and switch off the activity of the T cells, preventing them from attacking the cancer. By attaching to the receptor, cemiplimab prevents PD-L1 and PD-L2 from switching off the T cells, thereby increasing the ability of the immune system to kill cancer cells [1].  | **Authorized Indication:** **EMA:** cemiplimabas monotherapy is indicated for the treatment of adult patients with recurrent or metastatic cervical cancer and disease progression on or after platinum-based chemotherapy [1]. **Route of administration:** iv**Licensing status****EU CHMP P.O. date:** 13/10/2022**FDA M.A. date:** /**EU Speed Approval Pathway:**No**FDA Speed Approval Pathway:** /**-----ABBREVIATIONS:****AE**: adverse event**CI**: confidence interval**ECOG**: Eastern Cooperative Oncology Group**HR**: hazard ratio**M.A**.: marketing authorization**OS**: overall survival**P**: p-value**P.O**.: positive opinion**Pts**: patients**UTI**: urinary tract infection | **Summary of clinical EFFICACY:**EMPOWER-Cervical 1/GOG-3016/ENGOT-cx9 (NCT03257267) is a phase III, open-label, multicenter trial. The primary end-point was overall survival. Pts are women with recurrent or metastatic cervical carcinoma; they were eligible for participation if their tumor had progressed after platinum-containing therapy used to treat recurrence or metastases. Pts had to have previously received bevacizumab and paclitaxel therapy and previous bevacizumab treatment had to have been discontinued because of progression or toxic effects before enrollment in the trial. An ECOG performance status score of 0 or 1 was required for enrollment. Pts (n=608) were randomly\* assigned in a 1:1 ratio to receive either cemiplimab (n=304) or the investigator’s choice of chemotherapy\*\* as the control therapy (n=304); cemiplimab was administered at a flat dose of 350mg iv every 21 days for up to 96 weeks. In the overall population, median OS with cemiplimab was 12 months (95% CI, 10.3 to 13.5), as compared with 8.5 months (95% CI, 7.5 to 9.6) with chemotherapy (HR for death, 0.69; 95% CI, 0.56 to 0.84, two sided P<0.001). The OS benefit was consistent in both histologic subgroup (squamous-cell carcinoma and adenocarcinoma [including adenosquamous carcinoma]) [2].

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|  | Median overall survival  |
| cemiplimab | chemotherapy |
| Squamous-cell carcinomaHR 0.73; 95% CI, 0.58 to 0.91; two-sided P=0.006 | 11 months95% CI, 9.2 to 13.4 | 9 months95% CI, 7.6 to 9.8 |
| Adenocarcinoma or adenosquamous carcinomaHR, 0.56; 95% CI, 0.36 to 0.85 | 13 moths95% CI, 9.6 to 17.6  | 7 months95% CI, 5.1 to 9.7  |

\*Randomization was stratified according to histologic type (squamous-cell carcinoma or adenocarcinoma [including adenosquamous carcinoma]), previous bevacizumab exposure (yes or no), and ECOG performance-status score (0 or 1). \*\*n=111 were assigned to pemetrexed (500mg), n=121 to gemcitabine (1000mg), n=21 to topotecan (1mg), n=19 to irinotecan (100mg), n=32 to vinorebine. **Summary of clinical SAFETY:**The safety profile was consistent with that previously reported for the drug and for other PD-1 or PD-L1 inhibitors in pts with other tumor types. The number of deaths caused by AE was low in both treatment groups. The most common grade 3 or higher AE (occurring ≥5% of pts in either group) were anemia (12% with cemiplimab and 27% with chemotherapy), UTI (5% and 3%), and neutropenia (1% and 9%) [2].

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| **AE** | **Any** | **Serious** | **Led to discontinuation** | **Led to death\*** |
| Cemiplimab n(%) | Any grade | 265 (88%) | 89 (30%) | 26 (9%) | 5 (2%) |
| Grade 3,4 or 5 | 135 (30%) | 69 (23%) | 20 (7%) | 5 (2%) |
| Chemotherapy n(%) | Any Grade | 265 (91%) | 78 (27%) | 15 (5%) | 2 (1%) |
| Grade 3,4 or 5 | 155 (53%) | 64 (22%) | 11 (4%) | 2 (1%) |

\*None of AE leading to death were considered by the treating investigator to be related to cemiplimab. **Ongoing studies:*** ***For the same indication:***Yes
* ***For other indications:***Yes [3].

**Discontinued studies (for the same indication):** No | **Cost of therapy:**In Italy, the cost for Libtayo® 1 vial ev 350 mg is 6,626,25€ (ex-factory price) [4].**Epidemiology:**In Italy, cervical cancer represents the fifth most frequent cancer in women under 50 years of age and overall 1.3% of all those diagnosed [5]. -----**POSSIBLE PLACE IN THERAPY**Pembrolizumab in combination with chemotherapy with or without bevacizumab is approved in Italy for the treatment of persistent, recurrent or metastatic cervical cancer in adults with PDL-1 expressing tumor (score >1) [5-6].**OTHER INDICATIONS IN DEVELOPMENT**Basal cell cancer, Glioblastoma, Head and neck cancer, Liver cancer, Malignant melanoma, Non-small cell lung cancer, Oropharyngeal cancer, Prostate cancer, Squamous cell cancer [7]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:**No**OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:**Tisotumab vedotin\*Service reorganization: No\*Possible off label use: No-----**References:**[1]. <https://www.ema.europa.eu/en/medicines/human/summaries-opinion/libtayo-0>[2]. <https://doi.org/10.1016/j.annonc.2021.04.009>[3]. <https://adisinsight.springer.com/drugs/800042079>[4]. <https://gallery.farmadati.it/Home.aspx> [5]. <https://snlg.iss.it/wp-content/uploads/2022/09/LG-486-AIOM_Ca-Cervice-Endometrio.pdf>[6]. <https://gallery.farmadati.it/ViewDoc.aspx> [7]. <https://adisinsight.springer.com/drugs/800042079>[8]. Coleman RL, Lorusso D, Gennigens C, González-Martín A, Randall L, Cibula D, Lund B, Woelber L, Pignata S, Forget F, Redondo A, Vindeløv SD, Chen M, Harris JR, Smith M, Nicacio LV, Teng MSL, Laenen A, Rangwala R, Manso L, Mirza M, Monk BJ, Vergote I; innovaTV 204/GOG-3023/ENGOT-cx6 Collaborators. Efficacy and safety of tisotumab vedotin in previously treated recurrent or metastatic cervical cancer (innovaTV 204/GOG-3023/ENGOT-cx6): a multicentre, open-label, single-arm, phase 2 study. Lancet Oncol. 2021 May;22(5):609-619. doi: 10.1016/S1470-2045(21)00056-5. Epub 2021 Apr 9. PMID: 33845034.  |