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Keytruda (pembrolizumab): Restriction of indication for the treatment of locally advanced or metastatic urothelial carcinoma in adults who are not eligible for cisplatin-containing chemotherapy

Dear Healthcare Professional,

Merck Sharp & Dohme B.V. (MSD) in agreement with the European Medicines Agency and the Medicines Authority would like to inform you of the following:

Summary

- Preliminary data from an ongoing clinical trial (KEYNOTE-361) showed reduced survival with KEYTRUDA monotherapy compared to standard chemotherapy when used as first-line treatment for patients with locally advanced or metastatic urothelial carcinoma whose tumour has low expression of the protein programmed death-ligand 1 (PD-L1).
- As a result, the indication of KEYTRUDA for the treatment of locally advanced or metastatic urothelial carcinoma in adults who are not eligible for cisplatin-based chemotherapy is being changed as follows:

  "KEYTRUDA as monotherapy is indicated for the treatment of locally advanced or metastatic urothelial carcinoma in adults who are not eligible for cisplatin-containing chemotherapy and whose tumours express PD-L1 with a combined positive score (CPS) ≥10."
- The indication of KEYTRUDA for the treatment of locally advanced or metastatic urothelial carcinoma in adults who have received prior platinum-containing chemotherapy remains unchanged.

Background on the concern

KEYNOTE-361 is an ongoing Phase III, randomized, controlled, open-label clinical trial of pembrolizumab with or without platinum-based combination chemotherapy versus chemotherapy as first-line treatment in subjects with advanced or metastatic urothelial carcinoma.

Preliminary data from an early review showed a reduced survival with KEYTRUDA monotherapy in patients whose tumours express PD-L1 with a CPS < 10 compared with standard chemotherapy.

On 21st February 2018, based on a recommendation by the Data Monitoring Committee, MSD stopped the accrual in the KEYTRUDA monotherapy arm for patients whose tumours express PD-L1 with a CPS < 10. The KEYTRUDA monotherapy arm remains open only to patients whose tumours express PD-L1 with a CPS of ≥10. For subjects whose tumour express PD-L1 CPS <10 already enrolled into the KEYTRUDA monotherapy arm the decision regarding the continuation of study treatment is at the discretion of the investigator and participant. Randomisation to the chemotherapy and the chemotherapy-KEYTRUDA arms continues unaltered.

The DMC recommendations have also been communicated to EMA. Following review of these preliminary data by EMA, MSD has updated the product information for KEYTRUDA to limit pembrolizumab monotherapy for the treatment of locally advanced or metastatic urothelial carcinoma in adults who are not eligible for cisplatin-containing chemotherapy and whose tumours express PD-L1 with a combined positive score (CPS) ≥ 10.

Other approved indications for KEYTRUDA are not impacted.

Call for Reporting

Health care providers and patients should report adverse events in patients taking KEYTRUDA. You are asked to report suspected adverse reactions at ADR Reporting at: www.medicinesauthority.gov.mt/adrportal. Alternatively, adverse events should also be reported to Merck Sharp & Dohme Cyprus Ltd by calling **800 7 4433** or at **malta_info@merck.com**.

If you have any questions or require any additional information please contact Medical Information department of MSD at **800 7 4433** or at **malta_info@merck.com**

Yours sincerely,

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