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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 & Healthcare products Regulatory Agency (MHRA) would like to inform you of the following:

Summary

- Preliminary data from an ongoing clinical trial (KEYNOTE-361) showed reduced survival with pembrolizumab 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, randomised, 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 pembrolizumab 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 pembrolizumab monotherapy arm for patients whose tumours express PD-L1 with a CPS < 10. The pembrolizumab 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 pembrolizumab 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- pembrolizumab 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:

Keytruda ▼ is subject to additional monitoring. This will allow quick identification of new safety information. When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset and treatment dates.

Please report suspected adverse reactions with this medicine to the MHRA through the Yellow Card Scheme website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Alternatively, prepaid Yellow Cards for reporting are available:

- upon request by mail: "FREEPOST YELLOW CARD"
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- Or by electronic download through the Yellow Card section of the MHRA website

Company contact point:

If you have any questions, or if you require any further information, please contact the medical information service of:
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Yours sincerely,

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