Keytruda use restricted by the EMA because of low survival in some patients with low levels of cancer protein PD-L1

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Information on Keytruda

- Keytruda (pembrolizumab) is a medicinal product authorised in the EU for urothelial cancer (cancer of the bladder and urinary tract), melanoma (a skin cancer), non-small cell lung cancer and classical Hodgkin lymphoma (a blood cancer)
- Some cancer cells have a protein (PD-L1) which can attach to a receptor on immune cells (PD-1) and stop the immune cells from attacking them. Keytruda acts stopping the cancer from disabling the immune cells by targeting the receptor PD-1 on immune cells.

In Malta Keytruda is a centrally authorised product.

Information from the EMA about the safety concern

The Committee for Medicinal Products for Human Use (CHMP) finalised the review of Keytruda, started on 3rd May 2018, carried out as type II variation. Preliminary data from a clinical trial[1] showed reduced survival with Keytruda (pembrolizumab) when used as first-line treatment for urothelial cancer in patients with low levels PD-L1 protein. The EMA's recommendations are:

- The use of Keytruda should be restricted as first-line treatment of urothelial cancer in patients with high levels of PD-L1. There are no changes to how these medicines should be used in patients with urothelial cancer who have had chemotherapy or in patients with other cancers for which these medicines are approved
- The clinical trial is continuing but no new patients with low levels of PD-L1 will be given only Keytruda

The CHMP opinion will be forwarded to the European Commission, which will issue a final legally binding decision applicable in all EU Member States. A European Commission binding decision will be issued in due course

In Malta

For Healthcare Professionals

- Preliminary data from Keynote-361 show a reduced survival with Keytruda compared with chemotherapy in patients with locally advanced or metastatic urothelial cancer who have not received prior therapy and whose tumours have low expressions of PD-L1.

[1] Keynote-361

- Based on the data from the trial, which is still ongoing, the urothelial cancer indications for Keytruda is being revised as follows:

"Keytruda as monotherapy is indicated for the treatment of locally advanced or metastatic urothelial carcinoma in adults who have received prior platinum-containing chemotherapy (see section 5.1)"

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**

- There are no changes to the use of Keytruda in patients who have had chemotherapy for urothelial cancers or in patients with other cancers for which these medicines are approved.
- Healthcare professionals in the EU will be sent a letter with details of these recommendations and the ongoing study

Healthcare professionals prescribing Keytruda in the EU will receive a DHPC letter with further details once a European Commission decision will be issued. Archived DHPC letters are available online at http://www.medicinesauthority.gov.mt/dhpc.

Advice for Patients

- Ongoing studies show that Keytruda may not work well enough in some patients with cancer of the bladder and urinary tract.
- Keytruda will now only be used as a first treatment for this cancer in patients whose tests show a sufficient amount of a protein called PD-L1.
- If you have already had chemotherapy or have any other cancer, your treatment with Keytruda will continue as before.
- Speak to your doctor if you have any questions

For more information, please see the European Medicines Agency's Keytruda press release

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on Keytruda. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form (available from: **http://www.medicinesauthority.gov.mt/adrportal**) and sent by mail to Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 or email to postlicensing.medicinesauthority@gov.mt or to the marketing authorisation holder or their local representatives.

Post-Licensing Directorate
Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

Feedback Form

The Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health

The Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this formt (address side up), stapling the ends and then posting (no stamp required)

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