Date: 9th July 2018

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Direct Healthcare Professional Communication

Tecentriq® ▼ (atezolizumab): 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,
F. Hoffmann-La Roche Ltd in agreement with the European Medicines Agency and the Medicines and Healthcare products Regulatory Agency (MHRA) would like to inform you of the following:

Summary

- Preliminary data from an ongoing clinical trial (IMvigor130) show reduced survival with Tecentriq monotherapy compared to platinum based chemotherapy when used as first-line treatment for urothelial cancer patients with low expression of PD-L1.
- As a result, Tecentriq's first-line indication for urothelial cancer is being restricted. Tecentriq must now only be used for first-line treatment for urothelial cancer if the patient has **high expression of PD-L1** as follows:

  "*Tecentriq as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma (UC):*

  •after prior platinum-containing chemotherapy, or

  •who are considered cisplatin ineligible, ***and whose tumours have a PD-L1 expression ⩾ 5% (see section 5.1).***"
- The use of Tecentriq after prior chemotherapy remains unchanged.

Background on the efficacy concern

IMvigor130 is an ongoing phase III, multicentre, randomised, placebo-controlled study comparing platinum-based chemotherapy with atezolizumab administered as monotherapy or atezolizumab in combination with platinum-based chemotherapy in patients with untreated locally advanced or

metastatic urothelial carcinoma. IMvigor130 is enrolling patients in the first line setting who are both cisplatin eligible and cisplatin ineligible. The treatment arms are as follows:

- Arm A (atezolizumab in combination with platinum-based chemotherapy [cisplatin or carboplatin] and gemcitabine)
- Arm B (atezolizumab monotherapy)
- Arm C (placebo in combination with platinum-based chemotherapy [cisplatin or carboplatin] and gemcitabine)

Preliminary data showed a reduced survival with Tecentriq monotherapy compared to platinum based chemotherapy in patients with metastatic urothelial cancer who have not received prior therapy and whose tumours have low expression of the protein programmed death ligand 1 (PD-L1) (less than 5% of immune cells staining positive for PD-L1).

On 19th March 2018, the independent Data Monitoring Committee recommended that no new patients with low PD-L1 expression should be recruited in Arm B.

Patients already recruited in this arm will continue in the trial and patients with high PD-L1 expression (5% or greater of immune cells staining positive for PD-L1) will continue to be recruited in Arm B. Other arms of the trial (A and C) will continue as planned.

Call for reporting

Please continue to report suspected adverse drug reactions (ADR's) to the MHRA through the Yellow Card Scheme.

Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle▼

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

It is easiest and quickest to report ADRs online via the Yellow Cards website - https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store.

Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gsi.gov.uk
- 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 downloading and printing a form

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name.

Adverse events should also be reported to Roche Products Ltd. Please contact Roche Drug Safety Centre by emailing welwyn.uk_dsc@roche.com or calling +44 (0)1707 367554.

As Tecentriq is a biological medicine, healthcare professionals should report adverse reactions by brand name and batch number.

Company contact point

For further information or any questions please contact Roche Medical Information by phone on +44(0)800 328 1629 or via e-mail medinfo.uk@roche.com

Annexes

Prescribing Information for Tecentriq (atezolizumab) is available either via The European Medicines Agency website at http://www.ema.europa.eu/ema/, via the MHRA website at http://www.mhra.gov.uk/spc-pil/ or via the Electronic Medicines Compendium at http://www.medicines.org.uk/emc and will be updated.

Yours faithfully,

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