26th January 2024

Direct Healthcare Professional Communication (DHPC)

Exkivity▼ (mobocertinib) 40 mg hard capsules – Conditional Marketing Authorisation Withdrawal

Marketing Authorisation Number - PL 16189/0124

Dear Healthcare Professional,

Takeda UK Limited, in agreement with the Medicines and Healthcare products Regulatory Agency (MHRA), would like to inform you of the following:

Summary

- **The phase 3 confirmatory study (EXCLAIM-2; TAK-788-3001) of mobocertinib as a first-line treatment for patients with locally advanced or metastatic non–small cell lung cancer with EGFR Exon 20 insertion mutations did not confirm the clinical benefit of mobocertinib.**

- **There were no new safety concerns, however the trial did not meet its primary endpoint of progression free survival and therefore did not fulfil the obligations of the Conditional Marketing Authorisation granted in Great Britain.**

- **As a consequence, the Conditional Marketing Authorisation for Exkivity 40 mg hard capsules will be withdrawn from 8th March 2024.**

- **Following withdrawal of the Conditional Marketing Authorisation no new patients can be prescribed Exkivity.**

Background on the concern

Exkivity 40 mg hard capsules is indicated for the treatment of adult patients with epidermal growth factor receptor (EGFR) exon 20 insertion mutation-positive locally advanced or metastatic non-small cell lung cancer (NSCLC), who have received prior platinum-based chemotherapy. Exkivity was granted a Conditional Marketing Authorisation, and as a specific obligation of the license Takeda was required to provide results from study TAK-788-3001*, A Randomized Phase 3 Multicenter Open-label Study to Compare the Efficacy of TAK-788 as First-line Treatment Versus Platinum-Based Chemotherapy in Patients with Non–Small Cell Lung Cancer with EGFR Exon 20 Insertion Mutations* with the aim of confirming the clinical benefit of Exkivity.

The Independent Data Monitoring Committee (IDMC) for study TAK-788-3001 reviewed the efficacy and safety from an interim analysis undertaken during the study. There were no new safety concerns identified and the safety profile of Exkivity is consistent with its use as monotherapy indicated for the treatment of adult patients. However, the IDMC concluded that the primary endpoint of progression-free survival (PFS) met the pre-specified criteria for futility with a hazard ratio (HR) >1.0 (1.038). Given the absence of any other clinical trial capable of confirming the clinical benefit of Exkivity, Takeda will voluntarily withdraw the Conditional Marketing Authorisation for Exkivity in Great Britain.

For the Summary of Product characteristics, please visit https://www.medicines.org.uk/emc/product/13468/smpc#gref.

If you have patients currently receiving Exkivity:
With the agreement of the MHRA all patients who are currently deriving clinical benefit from treatment with Exkivity will have the opportunity to transition to a compassionate use program prior to withdrawal of the Conditional Marketing Authorisation.

Takeda has set up the compassionate use program with Clinigen and will maintain the Conditional Marketing Authorisation for Exkivity until 8th March 2024. Details have been provided below on how to enroll a patient on to the compassionate use program.

A few important notes about the compassionate use program:

- **General:** The Takeda programme will be managed by a third-party vendor, Clinigen and re-supply orders for ongoing patients from the point of the withdrawal will be placed via a Clinigen online portal.
- **Timing:** Takeda will begin enrolling patients into the compassionate use program starting February 1st 2024 to ensure a seamless transition with the goal of minimising disruption.
- **Eligibility**: Only patients prescribed Exkivity prior to the Conditional Marketing Authorisation withdrawal will be eligible for this compassionate use program. Exkivity will remain available for prescription up to the point of Conditional Marketing Authorisation withdrawal on 8th March 2024.

How to Enroll: Starting 1st February 2024, HCPs may enroll patient(s) who require continued access to Exkivity. Please see instructions below on how to create your Clinigen account and place a request.

1. To enroll your patient(s) currently prescribed Exkivity (mobocertinib) please email Clinigen Customer Service at medicineaccess@clinigengroup.com to create a Clinigen direct portal account. If you already have an account, you can log in through the link below:
    - https://onlineservices-identity.clinigengroup.com/
2. Once you are in the portal you will need to search for **Mobocertinib Compassionate Use Program** and click on "Enrol" which will direct you to complete the patient access form.
3. If you have questions regarding creating an account or placing your order, please email Clinigen Customer Service at medicineaccess@clinigengroup.com.

Call for reporting

Please continue to report suspected adverse drug reactions (ADRs) or suspected defective medicines 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 ▼

It is easiest and quickest to report ADRs online via the Yellow Card website - https://yellowcard.mhra.gov.uk/ or via the Yellow Card app available from the Apple App Store or Google Play Store.

Exkivity▼ (mobocertinib) is subject to additional monitoring. This will allow quick identification of new safety information.

Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.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
- by downloading and printing a form from the Yellow Card website (see link above)

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 Takeda: AE.GBR-IRL@takeda.com

Company contact point
Please contact Takeda at globaloncologymedinfo@takeda.com or telephone +44 (0) 3333 000 181

Any queries specifically related to the Clinigen online portal please contact: medicineaccess@clinigengroup.com or call us at one of the phone numbers listed here: https://www.clinigengroup.com/direct/en/contact-us/

For any further queries related to this update please contact your local Takeda contact.

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Yours faithfully,

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Takeda UK & Ireland