22nd June 2023

**Direct Healthcare Professional Communication (DHPC)**

# GAVRETO®▼(pralsetinib): Increased risk for tuberculosis and measures to minimise this risk

Dear Healthcare professional,

Roche Products Ltd, in agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA), would like to inform you of the following:

## *Summary*

- **Tuberculosis, mostly extrapulmonary, has been reported in patients receiving pralsetinib.**
- **Before starting treatment, patients should be evaluated for active and inactive ("latent") tuberculosis, as per local recommendations.**
- **In patients with active or latent tuberculosis, standard antimycobacterial therapy should be initiated before treatment with Gavreto is started.**

## *Background on the safety concern*

In the United Kingdom, Gavreto is subject to a conditional marketing authorisation. Gavreto is indicated as monotherapy for the treatment of adult patients with rearranged during transfection (RET) fusion-positive advanced non-small cell lung cancer (NSCLC) not previously treated with a RET inhibitor.

An investigation of global safety data for Gavreto identified 9 total cases of tuberculosis in pralsetinib-treated patients, of which the majority (7/9) occurred in tuberculosis-endemic regions. The events occurred in patients with and without prior known history of tuberculosis. In most cases, extrapulmonary tuberculosis was reported, such as lymph node tuberculosis, peritoneal tuberculosis, or renal tuberculosis.

Among patients treated in the ARROW trial (NCT03037385) (N=528) (for further information please visit clinicaltrials.gov), tuberculosis of any severity was reported in 4 (0.8%) patients, and a grade 3-4 event was reported in one patient (0.2%). This corresponds to a frequency of uncommon for tuberculosis (≥ 1/1,000 to < 1/100).

Roche Products Limited
M-GB-00012623
June 2023

6 Falcon Way, Shire Park
Welwyn Garden City AL7
1TW, United Kingdom

Registered in England
No.100674

Medical Information
Tel +44(0)800 328 1629
Email: medinfo.uk@roche.com

Before starting treatment, patients should be evaluated for active and inactive ("latent") tuberculosis, as per local recommendations. In patients with active or latent tuberculosis, standard antimycobacterial therapy should be initiated before treatment with Gavreto is started.

Co-administration of pralsetinib with strong CYP3A4 inducers, such as rifabutin or rifampicin, can decrease pralsetinib plasma concentrations, which may decrease the efficacy of pralsetinib.[1] Co-administration of pralsetinib with strong CYP3A4 inducers should be avoided. If co-administration cannot be avoided, increase the pralsetinib dose. For detailed information on dose modifications, please consult the Summary of Product Characteristics (SPC) available at:

Great Britain: https://www.medicines.org.uk/emc#gref

Northern Ireland: https://www.emcmedicines.com/en-gb/northernireland/

An update to product information to include the risk of tuberculosis and recommendations for testing and treatment is ongoing.

1. *Lee YP, Jeong BH, Eun Y, et al. Extrapulmonary tuberculosis in patients with RET fusion-positive non-small cell lung cancer treated with pralsetinib: A Korean single-centre compassionate use experience. Eur J Cancer. 2021;159:167-173. doi:10.1016/j.ejca.2021.09.037*

## *Call for reporting*

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

Please report ANY suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme.

Please report:

- All suspected ADRs associated with new drugs identified by the black triangle ▼

You can report via:

- the Yellow Card website
- the free Yellow Card app available from the Apple App Store or Google Play Store
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals

Alternatively, you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm.

Roche Products Limited
M-GB-00012623
June 2023

6 Falcon Way, Shire Park
Welwyn Garden City AL7
1TW, United Kingdom

Registered in England
No.100674

Medical Information
Tel +44(0)800 328 1629
Email: medinfo.uk@roche.com

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, timing 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.

## Company contact point

Should you have any questions regarding the use of Gavreto, please feel free to contact:

> Roche Medical Information by phone on +44(0)800 328 1629 or via e-mail medinfo.uk@roche.com

Thank you in advance for your understanding and cooperation in this additional information.

Yours faithfully,

Roche Products Limited

DocuSigned by:
Marius Scholtz
AB2CA8841CD144B...

Dr Marius Scholtz

Medical Cluster Lead/Chief Medical Officer