PLEASE READ

IMPORTANT MEDICINE SAFETY INFORMATION

APPROVED BY THE HPRA

An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

16th June 2023

Direct Healthcare Professional Communication (DHPC)

GAVRETO ▼ (pralsetinib): Increased risk for tuberculosis and measures to minimize this risk

Dear Healthcare professional,

Roche Products (Ireland) Limited in agreement with the European Medicines Agency (EMA) and the Health Products Regulatory Authority (HPRA) 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.**

Roche Products (Ireland) Limited

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Registered in Ireland
No. 214337

Background on the safety concern

In the European Union, 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 (N=528), 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).

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, rifampicin can decrease pralsetinib plasma concentrations, which may decrease the efficacy of pralsetinib. Co-administration of pralsetinib with strong CYP3A4 inducers should be avoided. If co-administration cannot be avoided, increase the pralsetinib dose.

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

Please ensure awareness of the content of this letter within your team.

Call for reporting

▼ 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. Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, website: www.hpra.ie.

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Healthcare professionals may also report any suspected adverse reactions with Gavreto (pralsetinib) to: the Drug Surveillance Centre in Roche Products (Ireland) Limited by telephone (01-4690700) or email (Ireland.drug_surveillance_centre@roche.com).

Company contact point

Should you have any questions regarding the use of Gavreto (pralstetinib), please feel free to contact us at: Medical Information at Roche Products (Ireland) Limited by telephone (01 4690700) or email (Ireland.druginfo@roche.com).

Yours sincerely,

DocuSigned by:
Abdul Al Khateeb
Signer Name: Abdul Al Khateeb
Signing Reason: I approve this document
Signing Time: 12-Jun-2023 | 2:48:53 PM CEST
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