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Important Risk Minimization Information

▼ Physician / Oncologist Communication on the most important risks associated with Portrazza (necitumumab); thromboembolic events and cardiorespiratory disorders

Dear Doctor,

Eli Lilly would like to inform you of important safety information on the key conditions for the safe use of necitumumab.

Necitumumab is a recombinant human monoclonal immunoglobulin G1 (IgG1) antibody that targets the epidermal growth factor receptor (EGFR). It is indicated in combination with gemcitabine and cisplatin chemotherapy for the treatment of adult patients with locally advanced or metastatic EGFR expressing squamous non-small cell lung cancer who have not received prior chemotherapy for this condition.

The information in this communication is based on clinical trial data at the time of marketing authorisation.

Summary

Thromboembolic events and cardiorespiratory disorders are the most important risks associated with necitumumab. The following information is important for the safe use of necitumumab and should be considered before treatment is initiated.

Thromboembolic events:

- Venous thromboembolic events (VTE) and arterial thromboembolic events (ATE), including fatal cases, were observed with necitumumab in combination with gemcitabine and cisplatin.
    - The incidence of VTE was 8.2% in patients receiving necitumumab plus gemcitabine and cisplatin versus 5.4% in patients receiving gemcitabine and cisplatin alone; for ATE, the incidence was 4.3% versus 3.9%. The incidence of fatal VTE was similar between arms (0.2%); the incidence of fatal ATE was 0.6% in the experimental arm versus 0.2% in the control arm.
- The relative risk of VTE or ATE was approximately three-fold higher in patients with a reported history of VTE or ATE. Administration of necitumumab should be

carefully considered in those patients with a history of thromboembolic events (such as pulmonary embolism, deep vein thrombosis, myocardial infarction, or stroke) or pre-existing risk factors for thromboembolic events (such as advanced age, patients with prolonged periods of immobilisation, severely hypovolaemic patients, or patients with acquired or inherited thrombophilic disorders).

- Necitumumab should not be administered to patients with multiple risk factors for thromboembolic events unless the benefits outweigh the risks to the patient.

- Thromboprophylaxis should be considered on an individual basis in those patients at higher risk of thromboembolism.

- Patients and physicians should be aware of signs and symptoms of thromboembolism. Patients should be instructed to seek medical care if they develop symptoms such as shortness of breath, chest pain, arm or leg swelling.

- Discontinuation of necitumumab in patients who experience a VTE or ATE should be considered after a thorough benefit risk assessment for the individual patient.

Cardiorespiratory disorders:

- An increased frequency of cardiorespiratory arrest or sudden death was observed with necitumumab in combination with gemcitabine and cisplatin.

    - Cardiorespiratory arrest or sudden death was reported in 2.8% (15/538) of patients treated with necitumumab compared to 0.6% (3/541) of patients treated with chemotherapy alone.

    - Twelve of the fifteen patients died within 30 days of the last dose of necitumumab and had comorbid conditions including history of coronary artery disease (n=3), hypomagnesaemia (n=4), chronic obstructive pulmonary disease (n=7), and hypertension (n=5). Eleven of the 12 patients had an unwitnessed death.

    - The incremental risk of cardiopulmonary arrest or sudden death in patients with a history of coronary artery disease, congestive heart failure, or arrhythmias as compared to those without these comorbid conditions is not known.

Further information on the safety concern and the recommendations

In order to familiarise yourself with all the safety concerns associated with necitumumab, please read this communication in conjunction with the enclosed Summary of Product Characteristics (SmPC).

It is important that patients are aware of the important risks associated with necitumumab and therefore please provide a copy of the patient information leaflet to your patients.

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 via Health Products Regulatory Authority (HPRA) Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. When reporting, please provide as much information as possible, including information about medical history, any concomitant medication, onset and treatment dates. Any suspected adverse reactions with necitumumab may also be reported to Lilly via telephone at 01 661 4377.

Company contact point

This letter is not intended as a complete description of the risks associated with the use of necitumumab. Please refer to the attached SmPC for a complete description of risks.

Please contact Lilly at: 01 661 4377 if you have any questions about the information in this letter or the safe and effective use of necitumumab.

Yours faithfully,

Eli Lilly and Company (Ireland) Limited

Enclosed:
Necitumumab Summary of Product Characteristics
Necitumumab Patient Information Leaflet