For the use of a registered oncologist only

OSIMERTINIB TABLETS

TAGRISSO™ 40 mg & 80 mg

Abbreviated Prescribing Information

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 80 mg tablet contains a dose of 80 mg osimertinib (as mesylate).

Each 40 mg tablet contains a dose of 40 mg osimertinib (as mesylate).

THERAPEUTIC INDICATIONS

TAGRISSO (osimertinib) is indicated for:

- the first-line treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.

- the treatment of patient with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive Non-small cell lung cancer (NSCLC), as detected by an appropriate test, whose disease has progressed on or after EGFR TKI therapy

POSOLOGY AND METHOD OF ADMINISTRATION

The recommended dose is 80 mg osimertinib once a day until disease progression or unacceptable toxicity. TAGRISSO can be taken with or without food at the same time each day.

CONTRAINDICATIONS

None

WARNINGS & PRECAUTIONS

- **Assessment of EGFR T790M mutation status -** A validated test should be performed in a clinical laboratory using either tumour tissue DNA or circulating tumour DNA (ctDNA) obtained from a plasma sample. Positive determination of EGFR mutation status (exon 19 deletions or exon 21 (L858R) substitution mutations for first-line treatment or T790M mutations following progression on or after EGFR TKI therapy) using either a tissue-based or plasma-based test indicates eligibility for treatment with TAGRISSO. However, if a plasma-based ctDNA test is used and the result is negative, it is advisable to follow-up with a tissue test wherever possible due to the potential for false negative results using a plasma-based test.
- **Interstitial lung disease (ILD) -** Withhold TAGRISSO and promptly investigate for ILD in any patient who presents with worsening of respiratory symptoms which may be indicative of ILD (e.g. dyspnea, cough and fever). Permanently discontinue TAGRISSO if ILD is confirmed. Please refer to full prescribing information.
- **QTc interval prolongation -** When possible, avoid use of TAGRISSO in patients with congenital long QT syndrome. Consider periodic monitoring with electrocardiograms (ECGs)

and electrolytes in patients with congestive heart failure, electrolyte abnormalities, or those who are taking medications that are known to prolong the QTc interval.

- **Changes in cardiac contractility -** In patients with cardiac risk factors and those with conditions that can affect LVEF, cardiac monitoring, including an assessment of LVEF at baseline and during treatment, should be considered. In patients who develop relevant cardiac signs/symptoms during treatment, cardiac monitoring including LVEF assessment should be considered.
- **Keratitis** - Patients presenting with signs and symptoms suggestive of keratitis such as acute or worsening: eye inflammation, lacrimation, light sensitivity, blurred vision, eye pain and/or red eye should be referred promptly to an ophthalmology specialist.

FERTILITY, PREGNANCY AND LACTATION

- Women of childbearing potential should be advised to avoid becoming pregnant while receiving TAGRISSO.
- TAGRISSO is not recommended during pregnancy and in women of childbearing potential not using contraception.
- Breast-feeding should be discontinued during treatment with TAGRISSO.
- Results from animal studies have shown that TAGRISSO has effects on male and female reproductive organs and could impair fertility.

UNDESIRABLE EFFECTS

The safety data of TAGRISSO reflect exposure to in 1142 patients with EGFR T790M mutation-positive non-small cell lung cancer. Most adverse reactions were Grade 1 or 2 in severity. The most commonly reported adverse drug reactions (ADRs) were diarrhoea (49%) and rash (47%). Grade 3 and Grade 4 adverse reactions with TAGRISSO were 9.7% and 0.9%, respectively. In patients treated with TAGRISSO 80 mg once daily, dose reductions due to adverse reactions occurred in 2.1 % of the patients. Discontinuation due to adverse reactions was 4.3%. Please refer to full prescribing information or detailed assessment of adverse events.

INTERACTIONS

It is recommended that concomitant use of strong CYP3A inducers with TAGRISSO should be avoided. If not possible, then increase TAGRISSO dose to 160 mg during the treatment with strong CYP3A inducer and resume at 80 mg, 3 weeks after discontinuation of the strong CYP3A inducer. No dose adjustments are required when TAGRISSO is used with moderate and/or weak CYP3A inducers. CYP3A4 inhibitors are not likely to affect the exposure of osimertinib. Gastric pH modifying agents can be concomitantly used with TAGRISSO without any restrictions. Patients taking concomitant medications with disposition dependent upon BCRP and with narrow therapeutic index should be closely monitored for signs of changed tolerability as a result of increased exposure of the concomitant medication whilst receiving TAGRISSO.

PHARMACOLOGICAL PROPERTIES

Mechanism of action

Osimertinib is a Tyrosine Kinase Inhibitor (TKI). It is an oral potent and selective irreversible inhibitor of Epidermal Growth Factor Receptors (EGFRs) harboring sensitising mutations (EGFRm) and TKI-resistance mutation T790M.

Pharmacokinetic properties

Based on population pharmacokinetic analysis, osimertinib apparent plasma clearance is 14.3 L/h, apparent volume of distribution is 918 L and terminal half-life of approximately 44 hours.

PHARMACEUTICAL PARTICULARS

EXCIPIENTS

Tablet core :- Mannitol, Microcrystalline cellulose, Low-substituted hydroxpropyl cellulose, Sodium stearyl fumarate.

Tablet coating:- Polyvinyl alcohol, Titanium dioxide, Macrogol 3350, Talc, Yellow iron oxide, Red iron oxide & Black iron oxide.

SHELF LIFE

2 years.

STORAGE

This medicinal product does not require any special storage conditions.

PRESENTATION

Film-coated tablet (tablet). The TAGRISSO 80 mg tablet is a beige, 7.25 x 14.5 mm, oval, biconvex tablet, debossed with "AZ" and "80" on one side and plain on the reverse.
The TAGRISSO 40 mg tablet is a beige, 9 mm, round, biconvex tablet, debossed with "AZ" and "40" on one side and plain on the reverse.

For full prescribing information, please contact:

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For more information, refer full prescribing Version 3, dated 13th April 2018.