Abbreviated Prescribing Information

Osimertinib Tablets

TAGRISSO™ 40 mg & 80 mg

COMPOSITION:

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

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

THERAPEUTIC INDICATIONS

Osimertinib is indicated for the treatment of patient with metstatic 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.

This medicinal product is for oral use. The tablet should be swallowed whole with water and it should not be crushed, split or chewed.

CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients listed in section pharmaceutical particulars.

St. John's wort should not be used together with TAGRISSO (Please refer to full prescribing information).

WARNINGS & PRECAUTIONS

- **Assessment of EGFR T790M mutation status -** A validated test should be performed using either tumour DNA derived from a tissue sample or circulating tumour DNA (ctDNA) obtained from a plasma sample.
- **Interstitial lung disease (ILD) -** Careful assessment of all patients with an acute onset and/or unexplained worsening of pulmonary symptoms (dyspnoea, cough, fever) should be performed to exclude ILD. Please refer to full prescribing information.
- **QTc interval prolongation -** QTc interval prolongation occurs in patients treated with TAGRISSO. QTc interval prolongation may lead to an increased risk for ventricular

tachyarrhythmias (e.g. torsade de pointes) or sudden death. No arrhythmic events were reported in AURAex or AURA2.

- **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.
- **Keratitis** - Patients presenting with signs and symptoms suggestive of keratitis 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 should not be used during pregnancy unless the clinical condition of the woman requires treatment with osimertinib.
- Breast-feeding should be discontinued during treatment with TAGRISSO.
- Results from animal studies have shown that osimertinib has effects on male and female reproductive organs and could impair fertility. Patients should be advised to use effective contraception for the following periods after completion of treatment with this medicinal product: at least 2 months for females and 4 months for males.

UNDESIRABLE EFFECTS

The safety data of TAGRISSO reflect exposure to TAGRISSO at a dose of 80 mg daily in 690 patients with EGFR T790M mutation-positive non-small cell lung cancer who received prior EGFR TKI therapy. Most adverse reactions were Grade 1 or 2 in severity. The most commonly reported adverse drug reactions (ADRs) were diarrhoea (44%) and rash (41%). Grade 3 and Grade 4 adverse events across both studies were 26% and 2%, respectively. In patients treated with TAGRISSO 80 mg once daily, dose reductions due to ADRs occurred in 2.3% of the patients. Discontinuation due to adverse reactions or abnormal laboratory parameters was 6.5%. 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. Moderate CYP3A4 inducers may also decrease osimertinib exposure and should be used with caution, or avoided when possible. 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 of the concomitant medication as a result of increased exposure whilst receiving TAGRISSO.

PHARMACOLOGICAL PROPERTIES

Mechanism of action

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

Pharmacokinetic properties

Osimertinib pharmacokinetic parameters have been characterized in healthy subjects and NSCLC patients. Based on population pharmacokinetic analysis, osimertinib apparent plasma clearance is

14.2 L/h, apparent volume of distribution is 986 L and terminal half-life of approximately 48 hours. The AUC and C_{max} increased dose proportionally over 20 to 240 mg dose range.

PHARMACEUTICAL PARTICULARS

Excipients

Tablet core :- Mannitol, Microcrystalline cellulose, Low-substituted hydroxypropyl cellulose & Sodium stearyl fumarate

Tablet coating:- Polyvinyl alcohol, Titanium dioxide (E 171), Macrogol 3350, Talc, Yellow iron oxide (E 172), Red iron oxide (E 172) & Black iron oxide (E 172)

Shelf life

2 years.

Storage

This medicinal product does not require any special storage conditions.

Presentation

Film-coated tablets.: 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.

Al/Al blisters containing 1x10 and 3x10 tablets.

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For more information, refer full prescribing Version 2, dated 29th May 2017