Osimertinib package insert pdf

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For people with certain types of EGFR+ non-small cell lung cancer (NSCLC), TAGRISSO is a targeted treatment option. Could TAGRISSO be right for your type of lung cancer? This information is intended for use by health professionals 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. See section 4.8 for how to report adverse reactions. TAGRISSO 40 mg film-coated tablets Each tablet contains 40 mg osimertinib (as mesylate). Excipient with known effect This medicine contains 0.3 mg sodium per 40 mg tablet. For the full list of excipients, see section 6.1. Film-coated tablet (tablet). Beige, 9 mm, round, biconvex tablet, debossed with “AZ” and “40” on one side and plain on the reverse. TAGRISSO as monotherapy is indicated for: • the adjuvant treatment after complete tumour resection in adult patients with stage IB-IIIA non-small cell lung cancer (NSCLC) whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations (see section 5.1). • the first-line treatment of adult patients with locally advanced or metastatic NSCLC with activating EGFR mutations. • the treatment of adult patients with locally advanced or metastatic EGFR T790M mutation-positive NSCLC. Treatment with TAGRISSO should be initiated by a physician experienced in the use of anticancer therapies. When considering the use of TAGRISSO, EGFR mutation status (in tumour specimens for adjuvant treatment and tumour or plasma specimens for locally advanced or metastatic setting) should be determined using a validated test method (see section 4.4). Posology The recommended dose is 80 mg osimertinib once a day. Patients in the adjuvant setting should receive treatment until disease recurrence or unacceptable toxicity. Treatment duration for more than 3 years was not studied. Patients with locally advanced or metastatic lung cancer should receive treatment until disease progression or unacceptable toxicity. If a dose of TAGRISSO is missed, the dose should be made up unless the next dose is due within 12 hours. TAGRISSO can be taken with or without food at the same time each day. Dose adjustments Dosing interruption and/or dose reduction may be required based on individual safety and tolerability. If dose reduction is necessary, then the dose should be reduced to 40 mg taken once daily. Dose reduction guidelines for adverse reactions toxicities are provided in Table 1. Table 1. Recommended dose modifications for TAGRISSO Target organ Adverse reactiona Dose modification Pulmonary ILD/Pneumonitis Discontinue TAGRISSO (see Section 4.4) Cardiac QTc interval greater than 500 msec on at least 2 separate ECGs Withhold TAGRISSO until QTc interval is less than 481 msec or recovery to baseline if baseline QTc is greater than or equal to 481 msec, then restart at a reduced dose (40 mg) QTc interval prolongation with signs/symptoms of serious arrhythmia Permanently discontinue TAGRISSO Other Grade 3 or higher adverse reaction Withhold TAGRISSO for up to 3 weeks If Grade 3 or higher adverse reaction improves to Grade 0-2 after withholding of TAGRISSO for up to 3 weeks TAGRISSO may be restarted at the same dose (80 mg) or a lower dose (40 mg) Grade 3 or higher adverse reaction that does not improve to Grade 0-2 after withholding for up to 3 weeks Permanently discontinue TAGRISSO a Note: The intensity of clinical adverse events graded by the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. ECGs: Electrocardiograms; QTc: QT interval corrected for heart rate Special populations No dosage adjustment is required due to patient age, body weight, gender, ethnicity and smoking status (see section 5.2). Hepatic impairment Based on clinical studies, no dose adjustments are necessary in patients with mild hepatic impairment (Child Pugh A) or moderate hepatic impairment (Child Pugh B). Similarly, based on population pharmacokinetic analysis, no dose adjustment is recommended in patients with mild hepatic impairment (total bilirubin ≤upper limit of normal (ULN) and aspartate aminotransferase (AST) >ULN or total bilirubin >1.0 to 1.5x ULN and any AST) or moderate hepatic impairment (total bilirubin between 1.5 to 3 times ULN and any AST). The safety and efficacy of this medicinal product has not been established in patients with severe hepatic impairment. Until additional data become available, use in patients with severe hepatic impairment is not recommended (see section 5.2). Renal impairment Based on clinical studies and population PK analysis, no dose adjustments are necessary in patients with mild, moderate, or severe renal impairment. The safety and efficacy of this medicinal product has not been established in patients with end-stage renal disease [creatinine clearance (CLcr) less than 15 mL/min, calculated by the Cockcroft and Gault equation], or on dialysis. Caution should be exercised when treating patients with severe and end-stage renal impairment (see section 5.2). Paediatric population The safety and efficacy of TAGRISSO in children or adolescents aged less than 18 years have not been established. No data are available. Method of administration This medicinal product is for oral use. The tablet should be swallowed whole with water and it should not be crushed, split or chewed. If the patient is unable to swallow the tablet, the tablet may first be dispersed in 50 mL of non-carbonated water. It should be dropped in the water, without crushing, stirred until dispersed and immediately swallowed. An additional half a glass of water should be added to ensure that no residue remains and then immediately swallowed. No other liquids should be added. If administration via nasogastric tube is required, the same process as above should be followed but using volumes of 15 mL for the initial dispersion and 15 mL for the residue rinses. The resulting 30 mL of liquid should be administered as per the naso-gastric tube manufacturer's instructions with appropriate water flushes. The dispersion and residues should be administered within 30 minutes of the addition of the tablets to water. Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. St. John's Wort should not be used together with TAGRISSO (see section 4.5). Assessment of EGFR mutation status When considering the use of TAGRISSO as adjuvant treatment after complete tumour resection in patients with NSCLC, it is important that the EGFR mutation positive status (exon 19 deletions (Ex19del) or exon 21 L858R substitution mutations (L858R)) indicates treatment eligibility. A validated test should be performed in a clinical laboratory using tumour tissue DNA from biopsy or surgical specimen. When considering the use of TAGRISSO as a treatment for locally advanced or metastatic NSCLC, it is important that the EGFR mutation positive status is determined. 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. Only robust, reliable and sensitive tests with demonstrated utility for the determination of EGFR mutation status should be used. Positive determination of EGFR mutation status (activating EGFR 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) Severe, life-threatening or fatal Interstitial Lung Disease (ILD) or ILD-like adverse reactions (e.g. pneumonitis) have been observed in patients treated with TAGRISSO in clinical studies. Most cases improved or resolved with interruption of treatment. Patients with a past medical history of ILD, drug-induced ILD, radiation pneumonitis that required steroid treatment, or any evidence of clinically active ILD were excluded from clinical studies (see section 4.8). Interstitial Lung Disease (ILD) or ILD-like adverse reactions (e.g. pneumonitis) were reported in 3.7% and were fatal in 0.3% (n=5) of the 1479 patients who received TAGRISSO in ADAURA, FLAURA and AURA studies. The incidence of ILD was 10.9% in patients of Japanese ethnicity, 1.6% in patients of Asian ethnicity and 2.5% in non-Asian patients (see section 4.8). 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. Treatment with this medicinal product should be interrupted pending investigation of these symptoms. If ILD is diagnosed, TAGRISSO should be discontinued and appropriate treatment initiated as necessary. Reintroduction of TAGRISSO should be considered only after careful consideration of the individual patient's benefits and risk. Stevens-Johnson syndrome Case reports of Stevens-Johnson syndrome (SJS) have been reported rarely in association with TAGRISSO treatment. Before initiating treatment, patients should be advised of signs and symptoms of SJS. If signs and symptoms suggestive of SJS appear, TAGRISSO should be interrupted or discontinued immediately. 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 ADAURA, FLAURA or AURA studies (see section 4.8). Patients with clinically important abnormalities in rhythm and conduction as measured by resting electrocardiogram (ECG) (e.g. QTc interval greater than 470 msec) were excluded from these studies (see section 4.8). When possible, the use of osimertinib in patients with congenital long QT syndrome should be avoided. Periodic monitoring with electrocardiograms (ECGs) and electrolytes should be considered in patients with congestive heart failure, electrolyte abnormalities, or those who are taking medicinal products that are known to prolong the QTc interval. Treatment should be withheld in patients who develop a QTc interval greater than 500 msec on at least 2 separate ECGs until the QTc interval is less than 481 msec or recovery to baseline if the QTc interval is greater than or equal to 481 msec, then resume TAGRISSO at a reduced dose as described in Table 1. Osimertinib should be permanently discontinued in patients who develop QTc interval prolongation in combination with any of the following: Torsade de pointes, polymorphic ventricular tachycardia, signs/symptoms of serious arrhythmia. Changes in cardiac contractility Across clinical trials, Left Ventricular Ejection Fraction (LVEF) decreases greater than or equal to 10 percentage points and a drop to less than 50% occurred in 3.2% (40/1233) of patients treated with TAGRISSO who had baseline and at least one follow-up LVEF assessment. 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. In a placebo controlled trial (ADAURA), 1.6% (5/312) of patients treated with TAGRISSO and 1.5% (5/331) of patients treated with placebo experienced LVEF decreases greater than or equal to 10 percentage points and a drop to less than 50%. Keratitis Keratitis was reported in 0.7% (n=10) of the 1479 patients treated with TAGRISSO in the ADAURA, FLAURA and AURA studies. 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 (see section 4.2 Table 1). Age and body weight Elderly patients (>65 years) or patients with low body weight (

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