EXAMPLE TREATMENT PLAN for TAGRISSO® (osimertinib) in combination with pemetrexed and platinum-based chemotherapy

This TAGRISSO Treatment Plan is a draft treatment plan for implementation of TAGRISSO in combination with pemetrexed and platinum-based chemotherapy into electronic medical records (EMRs) or paper treatment plans. Please modify as needed to meet institutional standards.

**Please see full** [**Prescribing Information**](https://www.azpicentral.com/pi.html?product=tagrisso) **for additional information.**

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| **Institution P&T Approval Date (if applicable):** |  |
| **Place in Therapy/Pathway:** |  |  |
| **Lead Physician:** | **Oncology Nurse/Pharmacist:** |  |
| **Approval Signature:** | **Approval Signature:** |  |

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| **Indication**  | **Comments** |
|  | * TAGRISSO, in combination with pemetrexed and platinum-based chemotherapy, is indicated for the first-line treatment of adult patients with locally advanced or metastatic NSCLC whose tumors have EGFR exon 19 deletions or exon 21 L858R mutations, as detected by an FDA-approved test.
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| **Contraindications** | None  |

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| **Drug (eRx)** | **Dosage** | **Comments** |
| Osimertinib 80 mgStrengths: 80 mg tablet, 40 mg tablet | * Recommended dose is an 80 mg tablet taken orally once daily when taken with pemetrexed and platinum-based chemotherapy.
* Refer to the Prescribing Information for pemetrexed and cisplatin or carboplatin for the respective dosing information.
* TAGRISSO may be taken with or without food.
* Treat patients with locally advanced or metastatic lung cancer until disease progression or unacceptable toxicity due to TAGRISSO.
* TAGRISSO is also available as a 40-mg tablet.
 | * Before initiating TAGRISSO in combination with pemetrexed and platinum-based chemotherapy, conduct cardiac monitoring in all patients, including assessment of left ventricular ejection fraction (LVEF)
* Before initiating TAGRISSO, perform complete blood count with differential.
* Instruct patients that if a dose of TAGRISSO is missed, do not make up for the missed dose. Take the next dose as scheduled.
* For patients who have difficulty swallowing solids:
	+ Disperse tablet in 60 mL (2 ounces) of noncarbonated water only. Stir until tablet is dispersed into small pieces (the tablet will not completely dissolve) and swallow immediately. Do not crush, heat, or ultrasonicate during preparation. Rinse the container with 120 mL to 240 mL (4 to 8 ounces) of water and immediately drink.
	+ If administration via nasogastric tube is required, disperse the tablet as above in 15 mL of noncarbonated water, and then use an additional 15 mL of water to transfer any residues to the syringe. The resulting 30 mL of liquid should be administered as per the nasogastric tube instructions with appropriate water flushes (approximately 30 mL)
	+ Store at 25°C (77°F), excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].
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| **Recommended Dosage****Modifications** | **Comments** |
| **Please see complete Prescribing Information for additional****information.** | When TAGRISSO is administered in combination with pemetrexed and platinum-based chemotherapy, modify the dose of any one of the treatments for the managements of adverse reactions, as appropriate. For TAGRISSO dose modification instructions, see below. Withhold, reduce the dose or permanently discontinue pemetrexed, cisplatin or carboplatin according to their respective Prescribing Information.**Dosage modifications for adverse reactions (ARs)****Pulmonary*** Interstitial lung disease (ILD)/pneumonitis: permanently discontinue TAGRISSO.

**Cardiac*** QTc interval >500 msec on at least 2 separate ECGs: withhold TAGRISSO until QTc interval is <481 msec or recovery to baseline if baseline QTc is ≥481 msec, then resume at 40-mg dose.
* QTc interval prolongation with signs/symptoms of life-threatening arrhythmia: permanently discontinue TAGRISSO.
* Symptomatic congestive heart failure: permanently discontinue TAGRISSO.

**Cutaneous*** Stevens-Johnson syndrome (SJS), Erythema Multiforme Major (EMM) and Toxic Epidermal Necrolysis (TEN): withhold TAGRISSO if suspected and permanently discontinue if confirmed.

**Blood and Bone Marrow*** Aplastic Anemia: Withhold TAGRISSO if suspected and permanently discontinue if confirmed.

**Other*** AR of Grade 3 or greater severity: withhold TAGRISSO for up to 3 weeks.
* If improvement to Grade 0-2 within 3 weeks: resume at 80 mg or 40 mg daily.
* If no improvement within 3 weeks: permanently discontinue TAGRISSO.

ARs graded by the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0.QTc=QT interval corrected for heart rate; ECG=electrocardiogram.**Dosage modifications for use with strong CYP3A4 inducers*** Avoid co-administering TAGRISSO with strong CYP3A inducers.
* Co-administering TAGRISSO with a strong CYP3A4 inducer decreased the exposure of osimertinib compared to administering TAGRISSO alone. Decreased osimertinib exposure may lead to reduced efficacy.
* If concurrent use is unavoidable, increase TAGRISSO dosage to 160 mg daily when co-administering with a strong CYP3A4 inducer. Resume TAGRISSO at 80 mg 3 weeks after discontinuation of the strong CYP3A4 inducer.
* No dose adjustments are required when TAGRISSO is used with moderate and/or weak CYP3A inducers.

CYP3A=cytochrome P450, family 3, subfamily A |

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|  | **Effects of TAGRISSO on other drugs** * Co-administering TAGRISSO with a breast cancer-resistant protein (BCRP) or P-glycoprotein (P-gp) substrate increased the exposure of the substrate compared to administering it alone. Increased BCRP or P-gp substrate exposure may increase the risk of exposure-related toxicity.
* Monitor for adverse reactions of the BCRP or P-gp substrate, unless otherwise instructed in its approved labeling when co-administered with TAGRISSO.

**Drugs that prolong the QTc interval*** The effect of co-administering medicinal products known to prolong the QTc interval with TAGRISSO is unknown.
* When feasible, avoid concomitant administration of drugs known to prolong the QTc interval with known risk of Torsades de pointes.
* If not feasible to avoid concomitant administration of such drugs, contact periodic ECG monitoring.

CYP3A=cytochrome P450, family 3, subfamily A; QTc=QT interval corrected for heart rate |

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| **Adverse Reactions** | **Comments** |
| **Please see complete Prescribing Information for additional****information on ARs.** | The most common (>20%) adverse reactions, including laboratory abnormalities, in TAGRISSO in combination with pemetrexed and platinum-based chemotherapy were leukopenia (88%), thrombocytopenia (85%), neutropenia (85%), lymphopenia (78%), rash (49%), diarrhea (43%), stomatitis (31%), nail toxicity (27%), dry skin (24%), and increased blood creatine (22%). |

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| **Warnings and Precautions** | **Comments** |
|  | **Interstitial Lung Disease (ILD)/Pneumonitis:** Withhold TAGRISSO and promptly investigate for ILD in patients who present with worsening of respiratory symptoms which may be indicative of ILD (e.g., dyspnea, cough and fever). Permanently discontinue TAGRISSO if ILD/pneumonitis is confirmed.* Interstitial lung disease (ILD)/pneumonitis occurred in 4% of the 1813 TAGRISSO-treated patients; 0.4% of cases were fatal.
* In the FLAURA2 study, ILD/pneumonitis occurred in 3.3% of the 276 patients who received TAGRISSO in combination with pemetrexed and platinum-based chemotherapy; 0.4% of cases were fatal.

**QTc Interval Prolongation:** Permanently discontinue TAGRISSO in patients who develop QTc interval prolongation with signs/symptoms of life-threatening arrhythmia* Heart rate-corrected QT (QTc) interval prolongation occurs in TAGRISSO-treated patients. Of the 1813 TAGRISSO monotherapy-treated patients in clinical trials, 1.1% were found to have a QTc >500 msec, and 4.3% of patients had an increase from baseline QTc >60 msec.
* Of the 276 patients treated with TAGRISSO in combination with pemetrexed and platinum-based chemotherapy in the FLAURA2 study, 1.8% were found to have a QTc >500 msec, and 10.5% of patients had an increase from baseline QTc >60 msec. No QTc-related arrhythmias were reported.
* Conduct periodic monitoring with ECGs and electrolytes in patients with congenital long QTc syndrome, congestive heart failure, electrolyte abnormalities, or those who are taking medications known to prolong the QTc interval.

**Cardiomyopathy:** Assess LVEF in patients who develop relevant cardiac signs or symptoms during treatment.For symptomatic congestive heart failure, permanently discontinue TAGRISSO.* Cardiomyopathy occurred in 3.8% of the 1813 TAGRISSO-treated patients; 0.1% of cardiomyopathy cases were fatal.
* In the FLAURA2 study, cardiomyopathy occurred in 9% of the 276 patients who received TAGRISSO in combination with pemetrexed and platinum-based chemotherapy; 1.1% of cardiomyopathy cases were fatal. A decline in left ventricular ejection fraction (LVEF) ≥10% from baseline and to <50% LVEF occurred in 4.2% of 1557 patients who had baseline and at least one follow-up LVEF assessment.
* In the ADAURA study, 1.5% (5/325) of TAGRISSO-treated patients experienced LVEF decreases ≥10% from baseline and a drop to <50%.
* In the FLAURA2 study, 8% (21/262) of patients treated with TAGRISSO in combination with pemetrexed and platinum-based chemotherapy, who had baseline and at least one follow-up LVEF assessment, experienced LVEF decreases ≥10% and a drop to less than 50%.
* For patients receiving TAGRISSO monotherapy, conduct cardiac monitoring in patients with cardiac risk factors, including assessment of LVEF at baseline and during treatment.
* For patients receiving TAGRISSO in combination with pemetrexed and platinum-based chemotherapy, conduct cardiac monitoring in all patients, including assessment of LVEF at baseline and during treatment.

**Keratitis:** Promptly refer patients with signs and symptoms suggestive of keratitis (such as eye inflammation, lacrimation, light sensitivity, blurred vision, eye pain and/or red eye) to an ophthalmologist.* Keratitis was reported in 0.6% of 1813 patients treated with TAGRISSO monotherapy in clinical trials.

**Erythema Multiforme Major, Stevens-Johnson Syndrome, and Toxic Epidermal Necrolysis:** Withhold TAGRISSO if erythema multiforme major (EMM), Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) is suspected and permanently discontinue if confirmed.* Postmarketing cases consistent with EMM, SJS and TEN have been reported in patients receiving TAGRISSO.

**Cutaneous Vasculitis:** Withhold TAGRISSO if cutaneous vasculitis is suspected, evaluate for systemic involvement, and consider dermatology consultation. If no other etiology can be identified, consider permanent discontinuation of TAGRISSO based on severity.* Postmarketing cases of cutaneous vasculitis including leukocytoclastic vasculitis, urticarial vasculitis, and IgA vasculitis have been reported in patients receiving TAGRISSO.

**Aplastic Anemia**: Perform complete blood count with differential before starting TAGRISSO, periodically throughout treatment, and more frequently if indicated. If aplastic anemia is suspected, withhold TAGRISSO and obtain a hematology consultation. If aplastic anemia is confirmed, permanently discontinue TAGRISSO. * Aplastic anemia has been reported in patients treated with TAGRISSO in clinical trials (0.06% of 1813) and postmarketing. Some cases had a fatal outcome. Inform patients of the signs and symptoms of aplastic anemia including but not limited to, new or persistent fevers, bruising, bleeding, and pallor.

**Embryo-Fetal Toxicity:** Verify pregnancy status of females of reproductive potential prior to initiating TAGRISSO.* Advise pregnant women of the potential risk to a fetus.
* Advise females of reproductive potential to use effective contraception during treatment with TAGRISSO and for 6 weeks after the final dose.
* Advise males with female partners of reproductive potential to use effective contraception for 4 months after the final dose.
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| **Use in Specific Populations** | **Comments** |
|  | **Pregnancy:** * Based on data from animal studies and its mechanism of action, TAGRISSO can cause fetal harm when administered to a pregnant woman. There are no available data on TAGRISSO use in pregnant women. Administration of TAGRISSO to pregnant rats was associated with embryolethality and reduced fetal growth at plasma exposures 1.5 times the exposure at the recommended clinical dose. Advise pregnant women of the potential risk to a fetus.
* In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

**Lactation:** * Due to the potential for serious adverse reactions in breastfed infants from osimertinib, advise women not to breastfeed during treatment with TAGRISSO and for 2 weeks after the final dose.

**Females and Males of Reproductive Potential*** Verify the pregnancy status of females of reproductive potential prior to initiating TAGRISSO.
* *Contraception*
	+ Advise females of reproductive potential to use effective contraception during treatment with TAGRISSO and for 6 weeks after the final dose.
	+ Advise males with female partners of reproductive potential to use effective contraception during and for 4 months after the final dose.
* *Infertility*
	+ Based on animal studies, TAGRISSO may impair fertility in females and males of reproductive potential.
	+ The effects on female fertility showed a trend toward reversibility. It is not known whether the effects on male fertility are reversible.

**Pediatric Use:** * The safety and effectiveness of TAGRISSO in pediatric patients have not been established.

**Geriatric Use:** * Of the 276 patients with EGFR exon 19 deletion or exon 21 L858R mutation-positive, locally advanced or metastatic NSCLC treated with TAGRISSO in combination with pemetrexed and platinum-based chemotherapy, 104 patients were ≥65 years and 23 patients were ≥75 years of age.
* Exploratory analysis suggests a higher incidence of Grade 3 or higher adverse reactions (68% vs 61%) and more frequent dosage modifications for adverse reactions (55% vs 43%) in patients 65 years or older as compared to those younger than 65 years.
* Clinical studies of TAGRISSO in combination with pemetrexed and platinum-based chemotherapy did not include sufficient numbers of patients age 65 and over to determine whether they respond differently from younger patients.

**Renal Impairment:** * No dose adjustment is recommended in patients with creatinine clearance [CLcr] 15-89 mL/min, as estimated by the Cockcroft Gault method.
* There is no recommended dose of TAGRISSO for patients with end-stage renal disease (CLcr <15 mL/min).

**Hepatic Impairment:** * No dose adjustment is recommended in patients with mild to moderate hepatic impairment (Child-Pugh A and B or total bilirubin ≤ upper limit of normal [ULN] and AST > ULN or total bilirubin between 1 to 3 times ULN and any AST).
* There is no recommended dose for TAGRISSO for patients with severe hepatic impairment (total bilirubin between 3 to 10 times ULN and any AST).
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| **Verification of Appropriate Plan/Drug/Dose/Pt:** | **Signature:** |
|  **RN Verification:**  |  |
| **Patient Verification:** |  |

Source: [TAGRISSO [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2024.]

Source URL: <https://www.azpicentral.com/pi.html?product=tagrisso>

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