



PDL DRUG REVIEW

Proprietary Name: Tagrisso®

Common Name: osimertinib

PDL Category: Antineoplastics Protein Tyrosine Kinase Inhibitors

<u>Comparable Products</u>	<u>Preferred Drug List Status</u>
Opdivo	N/A- medical coverage

Summary

Pharmacology/Usage: Osimertinib, the active ingredient of Tagrisso®, is a kinase inhibitor. Specifically, it is a kinase inhibitor of the epidermal growth factor receptor (EGFR), which binds irreversibly to certain mutant forms of EGFR (T790M, L858R, and exon 19 deletion) at about 9-fold lower concentrations than wild-type.

Indication: For the treatment of patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, who have progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

There is no pregnancy category associated with this product. However, based on data from animal studies and its mechanism of action, Tagrisso® can cause fetal harm when administered to a pregnant woman. There is no data available for use in pregnant women; however, administration to pregnant rats was associated with embryo lethality and reduced fetal growth at plasma exposures 1.5 times the exposure at the recommended human dose. It is recommended to advise pregnant women of the potential risk to a fetus. Furthermore, it is recommended to advise females of reproductive potential and male patients with female partners to use effective contraception during treatment and for 6 weeks after the final dose (females) and up to 4 months after the final dose (males). The safety and efficacy of use in the pediatric population have not been established.

Dosage Forms: Tablets: 40mg, 80mg

Recommended Dosage: It is recommended to confirm the presence of a T790M EGFR mutation in tumor specimens prior to starting treatment with Tagrisso®. Information on FDA-approved tests for the detection of T790M mutations is available at <http://www.fda.gov/companiondiagnostics>.

Take 80mg QD until disease progression or unacceptable toxicity. For those with difficulty swallowing solids, disperse tablet in 4 tablespoons of non-carbonated water only. Swallow or administer through a naso-gastric tube immediately. Rinse the container with 4-8 ounces of water and immediately drink or administer through the naso-gastric tube.

Please refer to the prescribing information for specific recommended dose modifications for adverse events, such as with pulmonary or cardiac events. Dose adjustments are not required for patients with mild to moderate renal impairment or for patients with mild hepatic impairment. There is no recommended dose for Tagrisso® for patients with severe renal or with moderate or severe hepatic impairment.

Drug Interactions: It is recommended to avoid concomitant use of Tagrisso® with strong CYP3A inhibitors (including macrolide antibiotics, antifungals, antivirals, nefazodone); however, if no other alternative is available, monitor closely for adverse reactions. It is recommended to avoid concomitant administration of Tagrisso® with

strong CYP3A inducers (e.g. phenytoin, rifampicin, carbamazepine, St. John's Wort). Last, it is recommended to avoid concomitant administration with drugs that are sensitive substrates of CYP3A, breast cancer resistance protein (BCRP), or CYP1A2 with narrow therapeutic indices (including but not limited to fentanyl, cyclosporine, quinidine, ergot alkaloids, phenytoin, or carbamazepine).

Common Adverse Drug Reactions: *There was no placebo data available to compare with Tagrisso® results.* The most frequently reported adverse events with Tagrisso® included diarrhea (42%), nausea (17%), decreased appetite (16%), constipation (15%), stomatitis (12%), rash (41%), dry skin (31%), nail toxicity (25%), pruritus (14%), eye disorders (18%), cough (14%), fatigue (14%), back pain (13%), headache (10%), pneumonia (4%), and venous thromboembolism (7%). Common laboratory abnormalities included hyponatremia (26%), hypermagnesemia (20%), lymphopenia (63%), thrombocytopenia (54%), anemia (44%), and neutropenia (33%).

Adverse events reported that may require dose modification include interstitial lung disease/pneumonitis, QTC interval prolongation, and cardiomyopathy.

Contraindications: There are currently no contraindications listed with this product.

Manufacturer: AstraZeneca Pharmaceuticals

Analysis: The efficacy of Tagrisso® was demonstrated in two multicenter, single-arm, open-label studies that included patients with metastatic EGFR T790M mutation-positive NSCLC who had progressed on prior systemic therapy, including an EGFR TKI. The main efficacy outcome for both trials was objective response rate (ORR). The table below includes results from both studies. Note that overall results were a pooled analysis of Study 1 and 2.

Efficacy Outcome	Study 1 (N=201)	Study 2 (N=210)	Overall (N=411)
ORR	57%	61%	59%
Complete Response	0	1%	0.5%
Partial Response	57%	60%	59%

In a separate dose finding section of Study 1, there were 63 patients with centrally confirmed T790M positive NSCLC who progressed on prior systemic therapy and were given Tagrisso® 80mg. In this population, the Blinded Independent Central Review (BICR)-confirmed ORR was 51%, and the median duration of response was 12.4 months from the time of first documented response.

Place in Therapy: Tagrisso® is indicated for the treatment of patients with metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer (NSCLC), as detected by an FDA-approved test, who have progressed on or after EGFR tyrosine kinase inhibitor (TKI) therapy. This indication is approved under accelerated approval based on tumor response rate and duration of response.

It is recommended that Tagrisso® require clinical prior authorization to verify diagnosis and prior trial/failure with EGFR tyrosine kinase inhibitor (TKI) therapy.

PDL Placement: Recommended
 Non-Recommended with Conditions

References

¹ Tagrisso [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals; 2015.