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IMPORTANT PRESCRIBING INFORMATION

TARCEVA® (erlotinib): Indications for maintenance and treatment after failure of at least one prior chemotherapy regimen are now modified for use only in patients with metastatic non-small cell lung cancer whose tumors harbor an EGFR exon 19 deletion or exon 21 (L858R) substitution mutation.

Dear Healthcare Professional,

OSI Pharmaceuticals, LLC, an affiliate of Astellas Pharma US, Inc. (Astellas) and Genentech USA, Inc. (Genentech) would like to inform you about important changes to the TARCEVA® (erlotinib) U.S. Prescribing Information (USPI).

Summary:

- **The previously approved indications for TARCEVA for the treatment of NSCLC have been modified and consolidated to a single indication as follows: “TARCEVA is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test receiving first-line, maintenance, or second or greater line treatment after progression following at least one prior chemotherapy regimen. [see USPI Clinical Studies (14.1, 14.3)]”.**

The Limitation of Use statement related to NSCLC with EGFR mutations other than exon 19 deletions or exon 21 (L858R) substitution mutations has been revised as follows: “Safety and efficacy of TARCEVA have not been established in patients with NSCLC whose tumors have other EGFR mutations [see USPI Clinical Studies (14.1, 14.2)]”.

- **In patients whose tumors do not harbor an EGFR exon 19 deletion or exon 21 (L858R) substitution mutation, TARCEVA is no longer indicated for maintenance therapy or treatment after progression following at least one prior chemotherapy regimen.**
- **The first-line indication remains the same and is approved for NSCLC patients with EGFR exon 19 deletions or exon 21 substitution mutations.**

Section 1.1 Indications and Usage of the USPI has been revised as indicated below.

Previous NSCLC indications

TARCEVA is indicated for:

- *First-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 substitution mutations as detected by an FDA-approved test [see USPI Clinical Studies (14.1)].*

- *The maintenance treatment of patients with locally advanced or metastatic non-small cell lung cancer whose disease has not progressed after four cycles of platinum-based first-line chemotherapy [see USPI Clinical Studies (14.2)].*
- *The treatment of patients with locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen [see USPI Clinical Studies (14.3)].*

New NSCLC indications and Limitation of use

TARCEVA is indicated for:

- *The treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test receiving first-line, maintenance, or second or greater line treatment after progression following at least one prior chemotherapy regimen [see USPI Clinical Studies (14.1, 14.3)].*

Limitation of use:

Safety and efficacy of TARCEVA have not been established in patients with NSCLC whose tumors have other EGFR mutations [see Clinical Studies (14.1, 14.2)].

Further information:

The IUNO study was a randomized, double-blind, placebo-controlled phase 3 study of first-line maintenance TARCEVA versus TARCEVA at the time of disease progression in patients with advanced or recurrent (Stage IIIB) or metastatic (Stage IV) NSCLC whose tumors did not harbor an EGFR- exon 19 deletion or exon 21 (L858R) mutation and who have not progressed following four cycles of platinum-based chemotherapy. Patients were randomized to receive maintenance TARCEVA or placebo. Following progression on initial therapy, patients were eligible to enter an open-label phase. Fifty percent of patients randomized to TARCEVA entered the open-label phase and received chemotherapy, while 77% of patients randomized to placebo entered the open-label phase and received TARCEVA.

Overall survival (OS) was not superior in patients randomized to receive maintenance TARCEVA compared to patients randomized to receive maintenance placebo [Hazard Ratio (HR) = 1.02 (95% Confidence Interval (CI), 0.85 to 1.22), p = 0.82]. Patients who received TARCEVA did not have superior progression-free survival (PFS) compared with patients who received placebo [HR 0.94 (95% CI 0.80 - 1.11), p = 0.48].

In this study, the reported safety profile of erlotinib is consistent with previously observed data in pivotal trials in NSCLC or as summarized in the TARCEVA USPI. Based on these data, no changes to the safety information in the USPI were required.

Other Information:

Medical Inquiries: Please contact Genentech Medical Communications at 1-800-821-8590.

Drug Safety/Adverse Events: In the event of any adverse health effects with this product, contact Genentech Drug Safety/Adverse Events at 1-888-835-2555.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

This letter is not intended as a complete description of the benefits and risks related to the use of TARCEVA. Please refer to the accompanying currently approved Full Prescribing Information.

Sincerely



Jeffery Bloss, MD
Senior Vice President, Medical Affairs Americas
Astellas Pharma Global Development, Inc.
for OSI Pharmaceuticals, LLC, an affiliate of
Astellas Pharma US, Inc.



Myriam Mendila, MD
Senior Vice President,
Head U.S. Medical Affairs
Genentech, Inc., a member of the Roche Group