



Complete guide to Tarceva dosing and administration

**Please see important safety information on pages 8-9
and enclosed full prescribing information.**

 **Tarceva**[®]
erlotinib
tablets

NSCLC dosing and administration

Tarceva indication and use in second-line advanced NSCLC

Tarceva monotherapy is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) after failure of at least one prior chemotherapy regimen.

Results from two multicenter, placebo-controlled, randomized, Phase III trials conducted in first-line patients with locally advanced or metastatic NSCLC showed no clinical benefit with the concurrent administration of Tarceva with platinum-based chemotherapy, and its use is not recommended in that setting.

- The recommended once-daily dose of Tarceva for use in advanced NSCLC is **150 mg taken orally**.¹
- Administering Tarceva above 150 mg daily may result in an unacceptable incidence of adverse events, such as diarrhea, rash, and liver transaminase elevation.¹

Dose adjustments in NSCLC

- If patients experience intolerable adverse events, such as intolerable skin reactions, intolerable diarrhea that is unresponsive to loperamide or that causes dehydration, or severe liver function test abnormalities, consider dose reduction or interruption of Tarceva.¹
- Patients with moderate/tolerable (Grade 2) or severe/intolerable (Grade ≥ 3) adverse reactions may be appropriate for treatment with medically managed supportive care.²



**Do not take
Tarceva
with food**

NSCLC dose adjustment guidelines

- Patients who smoke cigarettes while taking Tarceva should be advised to stop smoking, as cigarette smoking has been shown to reduce Tarceva exposure.¹
 - a Phase III study demonstrated that current smokers achieved Tarceva steady-state trough plasma concentrations that were approximately twofold less than those of former or never smokers
 - this effect was accompanied by a 24% increase in apparent Tarceva plasma clearance
 - in current smokers with NSCLC, pharmacokinetic analyses at steady-state indicated a dose-proportional increase in Tarceva exposure when the Tarceva dose was increased from 150 mg to 300 mg
- The exact dose recommended for smokers is unknown.¹
- If patients continue to smoke, a cautious increase in the dose of Tarceva, not exceeding 300 mg per day, may be considered while monitoring the patients' safety.¹
- Efficacy and long-term safety (>14 days) of a dose higher than the recommended starting dose have not been established in patients who continue to smoke.¹
- If patients decide to stop smoking while receiving a higher dose, the dose should be reduced immediately to the indicated starting dose.¹
- When dose reduction is necessary:
 - resume therapy at a 50-mg lower dose^{1,2}
 - in the clinical trials, the dose was held until symptom severity was Grade ≤1, and then therapy resumed at a 50-mg lower dose^{1,2}
 - in the clinical trials, 1% of patients receiving Tarceva discontinued due to rash¹
- Dose reduction is not appropriate if Interstitial Lung Disease (ILD), hepatic failure, or gastrointestinal perforation is diagnosed—Tarceva therapy should be discontinued. Interrupt or discontinue Tarceva in patients with dehydration who are at risk for renal failure, in patients with severe bullous, blistering, or exfoliative skin conditions, and in patients with acute/worsening ocular disorders.¹

NSCLC



150 mg

ONCE DAILY




100 mg

ONCE DAILY

If dose reduction is necessary, reduce by 50-mg decrements¹

Pancreatic cancer dosing & administration

Tarceva indication and use in first-line advanced pancreatic cancer

Tarceva in combination with gemcitabine is indicated for first-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer.

- The recommended once-daily dose of Tarceva is **100 mg taken orally in combination with gemcitabine.**¹
- In the Phase III pancreatic cancer trial, patients received the approved gemcitabine dose (1000 mg/m² IV) and schedule for pancreatic cancer.¹



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Pancreatic cancer dose adjustment guidelines

Dose adjustments in pancreatic cancer

- If patients experience intolerable adverse events, such as intolerable skin reactions, intolerable diarrhea that is unresponsive to loperamide or that causes dehydration, or severe liver function test abnormalities, consider dose reduction or interruption of Tarceva.¹
- Patients with moderate/tolerable (Grade 2) or severe/intolerable (Grade ≥ 3) adverse reactions may be appropriate for treatment with medically managed supportive care.²
- When dose reduction is necessary:
 - resume therapy at a 50-mg lower dose^{1,2}
 - in the clinical trials, the dose was held until symptom severity was Grade ≤ 1 , and then therapy resumed at a 50-mg lower dose^{1,2}
 - in the clinical trials, up to 1% of patients receiving Tarceva discontinued due to rash¹
- Dose reduction is not appropriate if Interstitial Lung Disease (ILD), hepatic failure, or gastrointestinal perforation is diagnosed—Tarceva therapy should be discontinued. Interrupt or discontinue Tarceva in patients with dehydration who are at risk for renal failure, in patients with severe bullous, blistering, or exfoliative skin conditions, and in patients with acute/worsening ocular disorders.¹



If dose reduction is necessary, reduce by a 50-mg decrement¹

Special considerations for pancreatic cancer

- Gemcitabine dose administration could be withheld or reduced for toxicities following the recommendations in the manufacturer's package insert.²

Other dosing information

- Erlotinib is metabolized predominantly by CYP3A4, and drugs that are CYP3A4 inhibitors or inducers may affect exposure and clearance of erlotinib.¹
- Erlotinib is metabolized to a lesser extent by CYP1A2. Drugs that are inhibitors of both CYP3A4 and CYP1A2 may increase exposure of erlotinib.¹
- Food substantially increases the bioavailability of erlotinib and may increase the risk of adverse events. Therefore, patients should be instructed to take Tarceva **at least one hour before or two hours after the ingestion of food.**¹⁻³
- The degree that food increases the bioavailability of erlotinib may vary; therefore, Tarceva tablets should be taken on an empty stomach to help ensure that patients obtain consistent plasma levels of the drug.^{1,2}
- In particular, **grapefruit** and **grapefruit juice** can significantly increase the bioavailability of erlotinib, so advise your patients to avoid them.⁴
- If the dose is missed, Tarceva can be taken during the same day at least one hour before or two hours after the ingestion of food.¹⁻³ If the daily dose is missed entirely, the regularly prescribed dose should be taken the next day. Do not double the dose of Tarceva.²
- To help minimize side effects, Tarceva should be taken **at least one hour before or two hours after meals.**



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Important safety information for NSCLC and pancreatic cancer

- There have been infrequent reports of serious Interstitial Lung Disease (ILD)-like events, including fatalities, in patients receiving Tarceva for treatment of NSCLC, pancreatic cancer or other advanced solid tumors. In the event of an acute onset of new or progressive, unexplained pulmonary symptoms such as dyspnea, cough and fever, Tarceva therapy should be interrupted pending diagnostic evaluation. If ILD is diagnosed, Tarceva should be discontinued and appropriate treatment instituted as needed.
- Cases of hepatic failure, hepatorenal syndrome, acute renal failure (all including fatalities), and renal insufficiency have been reported during use of Tarceva. Treatment with Tarceva should be used with extra caution in patients with total bilirubin $> 3 \times$ ULN. Tarceva dosing should be interrupted or discontinued if changes in liver function are severe. Patients should be closely monitored during therapy with Tarceva.
- Gastrointestinal perforation (including fatalities) has been reported in patients receiving Tarceva. Permanently discontinue Tarceva in patients who develop gastrointestinal perforation.
- Bullous, blistering and exfoliative skin conditions have been reported including cases suggestive of Stevens-Johnson syndrome/toxic epidermal necrolysis, which in some cases were fatal. Interrupt or discontinue Tarceva treatment if the patient develops severe bullous, blistering or exfoliating conditions.
- In the pancreatic cancer trial, other serious adverse reactions associated with Tarceva plus gemcitabine and which may have included fatalities, were myocardial infarction/ischemia, cerebrovascular accident and microangiopathic hemolytic anemia with thrombocytopenia.

- Corneal perforation and ulceration have been reported during use of Tarceva. Interrupt or discontinue Tarceva therapy if patients present with acute/worsening ocular disorders such as eye pain.
- When receiving Tarceva therapy, women should be advised against becoming pregnant or breastfeeding. Tarceva is pregnancy category D.
- The most common adverse reactions in patients with NSCLC receiving Tarceva monotherapy 150 mg were mild to moderate rash and diarrhea. Severe rash and diarrhea (9% & 6% NCI-CTC Grades 3–4, respectively) were reported. Rash and diarrhea each resulted in dose reductions (6% and 1%, respectively) and discontinuation in 1% of Tarceva-treated patients during the single-agent Phase III trial.
- The most common adverse reactions in patients with pancreatic cancer receiving Tarceva 100 mg plus gemcitabine were fatigue, rash, nausea, anorexia and diarrhea. Severe rash and diarrhea (5% and 5% NCI-CTC Grades 3–4, respectively) were reported. Rash and diarrhea each resulted in dose reductions in 2% of patients, and discontinuation in up to 1% of patients receiving Tarceva plus gemcitabine.

How supplied and storage information

How supplied

- Tarceva is available in 150-mg, 100-mg, and 25-mg strengths. Tarceva is supplied as white film-coated tablets for daily oral administration.¹

Tarceva 150-mg tablets

- Round, biconvex face and straight sides, white film-coated, printed in maroon with “T” and “150” on one side and plain on the other side.
- Supplied in bottles of 30 tablets (NDC 50242-064-01).



150 mg

Tarceva 100-mg tablets

- Round, biconvex face and straight sides, white film-coated, printed in gray with “T” and “100” on one side and plain on the other side.
- Supplied in bottles of 30 tablets (NDC 50242-063-01).



100 mg

Tarceva 25-mg tablets

- Round, biconvex face and straight sides, white film-coated, printed in orange with “T” and “25” on one side and plain on the other side.
- Supplied in bottles of 30 tablets (NDC 50242-062-01).



Storage

- Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F–86°F). See USP Controlled Room Temperature.

Tarceva dosing in second-line advanced NSCLC

- The recommended once-daily dose of Tarceva is 150 mg.¹

NSCLC



150 mg

Tarceva dosing in first-line advanced pancreatic cancer

- The recommended once-daily dose of Tarceva is 100 mg in combination with gemcitabine.¹

Pancreatic cancer



100 mg

Visit Tarceva.com for additional information and resources.

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References: **1.** Tarceva [package insert]. Melville, NY: OSI Pharmaceuticals Inc; 2009. **2.** Data on file, OSI Pharmaceuticals Inc. **3.** Hidalgo M, Siu LL, Nemunaitis J, et al. Phase I and pharmacologic study of OSI-774, an epidermal growth factor receptor tyrosine kinase inhibitor, in patients with advanced solid malignancies. *J Clin Oncol.* 2001;19(13):3267-3279. **4.** Huang SM, Lesko LJ. Drug-drug, drug-dietary supplement, and drug-citrus fruit and other food interactions: what have we learned? *J Clin Pharmacol.* 2004;44(6):559-569.

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Mixed Sources
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