


# Erlotinib (Tarceva)

**Drug type**

- Human epidermal growth factor receptor type 1/epidermal growth factor receptor (HER1/EGFR) tyrosine kinase inhibitor

## Indications

- Monotherapy for treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) after failure of at least one prior chemotherapy regimen
- Monotherapy for maintenance of patients with locally advanced or metastatic NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy
- In combination with gemcitabine (Gemzar) as first-line treatment of locally advanced, unresectable, or metastatic pancreatic cancer

## Unlabeled use

- Treatment of squamous cell head and neck cancer

## Mechanism of action

- Mechanism of action is not entirely understood
- HER1 and EGFR receptors are directly involved in intercellular signaling in systems governing cell division and proliferation
  - They are highly active and often overexpressed in rapidly dividing tumor cells
- By inhibiting the function of these receptors, erlotinib is thought to limit tumor cells' ability to divide and metastasize and may help initiate pathways of apoptotic cell death

## Dosage and administration

- Non-small cell lung cancer
  - 150 mg PO daily at least 1 hour before or 2 hours after food
  - Continue treatment until disease progression or unacceptable toxicity occurs
- Pancreatic cancer
  - 100 mg PO daily at least 1 hour before or 2 hours after food, in combination with gemcitabine
  - Continue treatment until disease progression or unacceptable toxicity occurs
- Dose modifications
  - When dose reduction is necessary, reduce the dose in 50-mg increments
  - In patients who develop acute onset of new or progressive pulmonary symptoms (eg, cough, dyspnea, fever), interrupt treatment pending diagnostic evaluation
  - If interstitial lung disease is diagnosed, discontinue erlotinib and institute appropriate treatment
  - Discontinue erlotinib for hepatic failure or GI perforation
  - Patients with dehydration who are at risk for renal failure, patients who develop severe skin reactions, patients who develop severe diarrhea unresponsive to loperamide or who become dehydrated, or patients with acute/worsening ocular disorders may require dose reduction or temporary interruption of therapy
- CYP-450 therapy
  - In patients receiving a strong CYP3A4 inhibitor or an inhibitor of both CYP3A4 and CYP1A2, consider a dose reduction
  - In patients receiving CYP3A4 inducers, alternative treatment lacking CYP3A4-inducing activity is strongly recommended
- If an alternative is unavailable, consider increasing the dose of erlotinib, as tolerated, at 2-wk intervals
- Reduce the erlotinib dose immediately after discontinuing the CYP3A4 inducer

- Cigarette smoking
  - Advise patients to stop smoking
  - In patients who continue to smoke, consider a cautious increase in dose of erlotinib up to 300 mg
- Safety and efficacy of doses higher than recommended starting dose not established in patients who continue to smoke for more than 14 days
  - Reduce dose of erlotinib immediately after cessation of smoking

### Pregnancy and lactation

- Pregnancy category D
  - Erlotinib may cause fetal harm when administered to a pregnant woman
- Excretion in breast milk is unknown

### Cautions and adverse effects

- Cautions
  - Hepatic function: Hepatic failure and hepatorenal syndrome (including fatalities) have been reported; use with caution, especially in patients with total bilirubin more than 3 times the upper limit of normal or Child-Pugh score A, B, and C; consider erlotinib dose reduction (in 50-mg increments), interruption, or discontinuation of therapy if severe changes in hepatic function develop
  - Cardiovascular effects: MI, ischemia, and stroke, including fatalities, have been reported
  - Dermatologic effects: Bullous, blistering, and exfoliative skin conditions have been reported, including cases (some fatal) of Stevens-Johnson syndrome/toxic epidermal necrolysis (TEN)
- Adverse effects
  - CNS: Fatigue
  - Dermatologic: Rash; pruritus; dry skin; acne; dermatitis acneiform; bullous, blistering, and exfoliative skin conditions (including cases of Stevens-Johnson syndrome/TEN)
  - Eyes, ears, nose, throat: Conjunctivitis, keratoconjunctivitis, corneal ulcerations or perforations, epistaxis, excessive growth and thickening of the eyelashes, hair and nail disorders including alopecia, hirsutism
  - GI: Diarrhea, anorexia, nausea, vomiting, stomatitis, abdominal pain, weight loss, GI bleeding, GI perforations
  - Genitourinary: Acute renal failure or renal insufficiency (including fatalities) with or without hypokalemia
  - Hepatic: Hepatic failure, elevated bilirubin, and ALT
  - Respiratory: Dyspnea, cough

### Drug interactions

- CYP inducers (eg, carbamazepine, phenobarbital, phenytoin, rifabutin, rifampin, rifapentine, St. John's wort) may reduce erlotinib plasma concentrations, decreasing the therapeutic effect and necessitating dosage adjustments or changes in therapy (see Dose modifications above)
- Use with caution with strong CYP3A4 inhibitors (atazanavir, clarithromycin, grapefruit or grapefruit juice, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, troleandomycin, voriconazole)
  - Erlotinib plasma concentrations may be elevated, increasing the risk of adverse reactions and necessitating dosage reduction
- Drugs that alter upper GI tract pH (eg, antacids, H2 receptor antagonists [eg, ranitidine], proton pump inhibitors [PPIs] [eg, omeprazole])
  - Avoid coadministration of erlotinib and PPIs
  - Separate erlotinib and antacid dosing by several hours
  - Administer erlotinib 10 hours after the H2 receptor antagonist and at least 2 hours before the next H2 antagonist dose
- Use with caution with drugs that inhibit both CYP1A2 and CYP3A4 (eg, ciprofloxacin)
  - Erlotinib plasma concentrations may be elevated, increasing the risk of adverse reactions and necessitating dosage reduction
- The bioavailability of erlotinib is substantially increased by food to almost 100%
  - Administer erlotinib at least 1 hour before or 2 hours after food
- Warfarin
  - International normalized ratio (INR) elevations and bleeding have been reported with erlotinib coadministration
  - Monitor prothrombin time (PT) and INR, and adjust warfarin dose as needed

### Monitoring

- Monitor for dermatologic, GI, ophthalmic, respiratory, and general body adverse reactions
- Periodic liver function tests are recommended
- Periodic monitoring of renal function and serum electrolytes is recommended for patients at risk of dehydration

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- Monitor for acute onset or progression of pulmonary symptoms (eg, cough, dyspnea, fever)
- Monitor PT and INR regularly in patients taking warfarin or other coumarin-derivative anticoagulants

**What to tell your patient**

- You have been prescribed erlotinib, which is designed to block tumor cell growth by targeting a protein called EGFR (epidermal growth factor) that is present on the surface of some cancer cells and some normal cells. Erlotinib inhibits an enzyme within the cell (tyrosine kinase) that is associated with EGFR. Erlotinib is given in tablet form to be taken by mouth at least 1 hour before or 2 hours after eating. The tablets are supplied in 25-mg, 100-mg, and 150-mg strengths.
- Side effects of erlotinib
  - Remember that your doctor has prescribed this medication because he or she has judged that the benefit is greater than the risk of side effects
  - Most people do not experience all of the side effects listed
  - Side effects are often predictable in terms of their onset and duration
  - Side effects are almost always reversible and will go away after treatment
  - There are many ways to minimize or prevent side effects
- The following side effects are common for patients taking erlotinib: rash, diarrhea, poor appetite, fatigue, shortness of breath, cough, and nausea and vomiting
- These side effects are less common for patients taking erlotinib: infection, mouth sores, itching, dry skin, eye irritation, and abdominal pain
- Contact your nurse or doctor immediately, day or night, if you should experience onset or worsening of unexplained shortness of breath or cough
- The following symptoms require medical attention but are not an emergency; contact your nurse or doctor within 24 hours of noticing any of the following:
  - Nausea (interferes with ability to eat and unrelieved with prescribed medication)
  - Vomiting (vomiting more than 4 to 5 times in a 24-hour period)
  - Diarrhea (4 to 6 episodes in a 24-hour period)
  - Extreme fatigue that prevents self-care activities
  - Mouth sores/skin rash (painful redness, swelling, or ulcers)
  - Eye irritation
  - Inability to eat or drink for 24 hours or have signs of dehydration: tiredness, thirst, dry mouth, dark and decreased amount of urine, or dizziness
- Precautions
  - Because certain medications can interfere with the levels/effects of erlotinib, be sure to tell your oncologist all medications you are taking
  - Tell your nurse or doctor what herbal products you are taking, especially St. John's wort
  - Do not take aspirin or products containing aspirin unless your doctor specifically permits this
  - Avoid eating grapefruit and drinking grapefruit juice while taking erlotinib
  - Do not receive any kind of immunization or vaccination without your doctor's approval while taking erlotinib
  - Inform your nurse or doctor if you are pregnant or may be pregnant prior to starting this treatment
  - For both men and women: Do not conceive a child (get pregnant) while taking erlotinib; barrier methods of contraception, such as condoms, are recommended
  - Do not breast-feed while taking this medication
- Self-care tips
  - Take erlotinib on an empty stomach, 1 hour before or 2 hours after eating
  - If you are taking antacids, take them several hours before or several hours after you take erlotinib
  - Drink at least 2 to 3 quarts of fluid every 24 hours, unless you are instructed otherwise
  - To prevent diarrhea that may be caused by erlotinib, drink small sips of a liquid such as a sugar-free sports drink often throughout the day, eat mild foods such as crackers and toast, and avoid spicy foods
  - You may be at risk of infection; report fever or any other signs of infection immediately
  - To help treat/prevent mouth sores, use a soft toothbrush, and rinse three times a day with 1/2 to 1 teaspoon of baking soda and/or 1/2 to 1 teaspoon of salt mixed with 8 ounces of water
  - To reduce nausea, take the antinausea medications your doctor prescribed and eat small, frequent meals
  - Avoid sun exposure; wear SPF 15 or higher sunblock and protective clothing
  - Drinking alcohol should be minimized or avoided; discuss this with your nurse or doctor
  - Get plenty of rest
  - Maintain good nutrition ■

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