Erlotinib

Class:
Antineoplastic Agent, Tyrosine Kinase Inhibitor; Growth Factor Receptor (EGFR) Inhibitor.

Indications:
Non small cell lung cancer (NSCLC)
Pancreatic cancer

Available dosage form in the hospital:
150 mg TAB

Trade Names: Tarceva

Doses:
- **Non small cell lung cancer (NSCLC), metastatic, first-line therapy in patients with EGFR exon 19 deletions or exon 21 (L858R) substitution mutations:** Oral: 150 mg once daily until disease progression or unacceptable toxicity
-**NSCLC, refractory:** Oral: 150 mg once daily until disease progression or unacceptable toxicity (Shepherd, 2005)
-**NSCLC, maintenance therapy:** Oral: 150 mg once daily until disease progression or unacceptable toxicity
-**Pancreatic cancer:** Oral: 100 mg once daily until disease progression or unacceptable toxicity (in combination with gemcitabine) (Moore, 2007)
-**Dosage adjustment for concomitant CYP3A4 inhibitors/inducers:**
-*CYP3A4 inhibitors:* Avoid concurrent use if possible; consider dose reductions for severe adverse reactions if erlotinib is administered concomitantly with strong CYP3A4 inhibitors (eg, azole antifungals, clarithromycin, erythromycin, nefazodone, protease inhibitors, telithromycin). Dose reduction (if required) should be done in decrements of 50 mg (after toxicity has resolved to baseline or ≤ grade 1).
-*Concomitant CYP3A4 and CYP1A2 inhibitor (eg, ciprofloxacin):* Avoid concurrent use if possible; consider dose reductions in decrements of 50 mg if severe adverse reactions occur (after toxicity has resolved to baseline or ≤ grade 1).
-*CYP3A4 inducers:* Alternatives to the enzyme-inducing agent should be utilized first. Concomitant administration with CYP3A4 inducers (eg, carbamazepine, phenobarbital, phenytoin, rifamycins, and St John's wort) may require increased erlotinib doses (increase as tolerated at 2-week intervals in 50 mg increments to a maximum of 450 mg); doses >150 mg daily should be considered with rifampin (the maximum erlotinib dose studied in combination with rifampin was 450 mg). Immediately reduce erlotinib dose to recommended starting dose when CYP3A4 inducer is discontinued.
-**Dosage adjustment for concomitant smoking:** Increase dose at 2-week intervals in 50 mg increments to a maximum dose of 300 mg (with careful monitoring) in patients who continue to smoke; immediately reduce erlotinib dose to recommended starting dose upon smoking cessation.

Geriatric
Refer to adult dosing.

Renal Impairment:

-*Renal impairment at treatment initiation:* No dosage adjustment provided in the manufacturer's labeling (has not been studied), although <9% of a single dose is excreted in the urine.

- **Renal toxicity during treatment**: Withhold treatment for grades 3/4 renal toxicity (consider discontinuing) and for risk of renal failure due to dehydration; may resume after euvolemia re-established (at previous dose). If treatment withheld due to toxicity and therapy is resumed, reinitiate with a 50 mg dose reduction after toxicity has resolved to baseline or ≤ grade 1..

Hepatic impairment:

Hepatic impairment at treatment initiation:

-U.S. labeling:

- Total bilirubin > ULN or Child-Pugh classes A, B, and C: No dosage adjustment provided in manufacturer's labeling; use with caution and monitor closely during treatment.
- Total bilirubin >3 times ULN: Use extreme caution.

-Canadian labeling:

- Moderate impairment: No dosage adjustment provided in manufacturer's labeling; however, a reduced dose should be considered.
- Severe impairment (including total bilirubin >3 times ULN and/or transaminases >5 times ULN): Use is not recommended

The following adjustments have also been studied: A reduced starting dose (75 mg once daily) has been recommended in patients with hepatic dysfunction (AST ≥3 times ULN or direct bilirubin 1-7 mg/dL), with individualized dosage escalation if tolerated (Miller, 2007); another study determined that pharmacokinetic and safety profiles were similar between patients with normal hepatic function and moderate hepatic impairment (O'Bryant, 2012).

Hepatotoxicity during treatment: U.S. labeling:

- Patients with normal hepatic function at baseline: If total bilirubin >3 times ULN and/or transaminases >5 times ULN during use: Interrupt therapy (consider discontinuing); if treatment is resumed, reinitiate with a 50 mg dose reduction after bilirubin and transaminases return to baseline; discontinue treatment if there is no significant improvement or resolution within 3 weeks.
- Patients with baseline hepatic impairment or biliary obstruction: If bilirubin doubles or transaminases triple over baseline during use: Interrupt therapy (consider discontinuing); if treatment is resumed, reinitiate with a 50 mg dose reduction after bilirubin and transaminases return to baseline; discontinue treatment if there is no significant improvement or resolution of hepatotoxicity within 3 weeks.

Dosing: Adjustment for Toxicity

-*Dermatologic toxicity:*

- Bullous, blistering or exfoliative skin toxicity (severe): Discontinue treatment.
- Severe rash (unresponsive to medical management): Withhold treatment; may reinitiate with a 50 mg dose reduction after toxicity has resolved to baseline or ≤ grade 1.

-*Gastrointestinal toxicity:*

- Diarrhea: Manage with loperamide; in severe diarrhea (unresponsive to loperamide) or dehydration due to diarrhea, withhold treatment; may reinitiate with a 50 mg dose reduction after toxicity has resolved to baseline or ≤ grade 1.
- Gastrointestinal perforation: Discontinue treatment.

-*Ocular toxicities:*

- Acute or worsening ocular toxicities (eg, eye pain): Interrupt and consider discontinuing treatment. If therapy is resumed, reinitiate with a 50 mg dose reduction after toxicity has resolved to baseline or ≤ grade 1.
- Corneal perforation or severe ulceration: Discontinue treatment.
- Keratitis (grade 3 or 4 or grade 2 persisting >2 weeks): Withhold treatment; may reinitiate with a 50 mg dose reduction after toxicity has resolved to baseline or ≤ grade 1.

-*Pulmonary symptoms:* Acute onset (or worsening) of pulmonary symptoms (eg, dyspnea, cough, fever): Interrupt treatment and evaluate for drug-induced interstitial lung disease; discontinue permanently with development of interstitial lung disease

Common side effect:

Cardiovascular: Chest pain (≤18%)

Central nervous system: Fatigue (9% to 52%)

Dermatologic: Skin rash (49% to 85%; grade 3: 5% to 13%; grade 4: <1%; median onset: 8 days), xeroderma (4% to 21%), paronychia (4% to 16%), alopecia (14% to 15%), pruritus (7% to 16%), acne vulgaris (6% to 12%)

Gastrointestinal: Diarrhea (20% to 62%; grade 3: 2% to 6%; grade 4: <1%; median onset: 12 days), anorexia (9% to 52%), nausea (23% to 33%), decreased appetite (≤28%), vomiting (13% to 23%), Stomatitis (11% to 17%), mucositis (≤18%), abdominal pain (3% to 11%), constipation (≤8%)

Genitourinary: Urinary tract infection (≤4%)

Hematologic & oncologic: Anemia (≤11%; grade 4: 1%)

Infection: Increased susceptibility to infection (4% to 24%)

Neuromuscular & skeletal: Weakness (≤53%), back pain (19%), arthralgia (≤13%), musculoskeletal pain (11%)

Ophthalmic: Conjunctivitis (12% to 18%), keratoconjunctivitis sicca (12%)

Respiratory: Cough (33% to 48%), dyspnea (41% to 45%; grades 3/4: 8% to 28%)

Miscellaneous: Fever (≤11%)

Pregnancy Risk Factor: D