Lapatinib: Drug information

(For additional information see "Lapatinib: Patient drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

ALERT: US Boxed Warning

Hepatotoxicity:

Hepatotoxicity has been observed in clinical trials and postmarketing experience. The hepatotoxicity may be severe, and deaths have been reported. Causality of the deaths is uncertain.

Brand Names: US

Tykerb

Brand Names: Canada

Tykerb

Pharmacologic Category

Antineoplastic Agent, Anti-HER2; Antineoplastic Agent, Epidermal Growth Factor Receptor (EGFR) Inhibitor; Antineoplastic Agent, Tyrosine Kinase Inhibitor

Dosing: Adult

Breast cancer, metastatic, HER2+ (with prior anthracycline, taxane, and trastuzumab therapy): Oral: 1,250 mg once daily (in combination with capecitabine) until disease progression or unacceptable toxicity (Geyer 2006)

Breast cancer, metastatic, HER2+, hormonal therapy indicated: Oral: 1,500 mg once daily (in combination with letrozole) until disease progression (Johnston 2009)

Breast cancer, metastatic, HER2+ with brain metastases, first-line therapy (off-label use): Oral: 1,250 mg once daily (in combination with capecitabine) until disease progression or unacceptable toxicity (Bachelot 2013)

Breast cancer, metastatic, HER2+, with progression on prior trastuzumab therapy (off-label use): Oral: 1,000 mg once daily (in combination with trastuzumab) (Blackwell 2010; Blackwell 2012)

Missed doses: If a dose is missed, resume with the next scheduled daily dose; do not double the dose the next day.

Dosage adjustment for concomitant CYP3A4 inhibitors/inducers:

CYP3A4 inhibitors: Avoid the use of concomitant strong CYP3A4 inhibitors. If concomitant use cannot be avoided, consider reducing lapatinib to 500 mg once daily with careful monitoring. When a strong CYP3A4 inhibitor is discontinued, allow ~1 week to elapse prior to adjusting the lapatinib

dose upward.

CYP3A4 inducers: Avoid the use of concomitant strong CYP3A4 inducers. If concomitant use cannot be avoided, consider gradually titrating lapatinib from 1,250 mg once daily up to 4,500 mg daily (in combination with capecitabine) **or** from 1,500 mg once daily up to 5,500 mg daily (in combination with letrozole), based on tolerability and with careful monitoring. If the strong CYP3A4 enzyme inducer is discontinued, reduce the lapatinib dose to the indicated dose.

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

There are no dosage adjustments provided in the manufacturer's labeling (has not been studied); however, due to the minimal renal elimination (<2%), dosage adjustments may not be necessary.

Dosing: Hepatic Impairment

Mild or moderate preexisting impairment (Child-Pugh class A or B): There are no dosage adjustments provided in the manufacturer's labeling.

Severe preexisting impairment (Child-Pugh class C): The following adjustments should be considered (and are predicted to normalize the AUC), however, there are no clinical data associated with the adjustments.

In combination with capecitabine: Reduce dose from 1,250 mg once daily to 750 mg once daily.

In combination with letrozole: Reduce dose from 1,500 mg once daily to 1,000 mg once daily.

Severe hepatotoxicity during treatment: Discontinue permanently (do not rechallenge).

Dosing: Adjustment for Toxicity

Cardiac toxicity: Discontinue treatment for at least 2 weeks for LVEF < LLN or decreased LVEF ≥ grade 2; may be restarted at 1,000 mg once daily (in combination with capecitabine) **or** 1,250 mg once daily (in combination with letrozole) if LVEF recovers to normal and patient is asymptomatic.

Dermatologic toxicity: Discontinue treatment for suspected erythema multiforme, Stevens-Johnson syndrome, or toxic epidermal necrolysis.

Diarrhea:

Grade 3 diarrhea or grade 1 or 2 diarrhea with complicating features (moderate-to-severe abdominal cramping, grade 2 or higher nausea/vomiting, decreased performance status, fever, sepsis, neutropenia, frank bleeding, or dehydration): Interrupt treatment; may restart at a reduced dose (from 1,500 mg once daily to 1,250 mg once daily or from 1,250 mg once daily to 1,000 mg once daily) when diarrhea resolves to ≤ grade 1.

Grade 4 diarrhea: Permanently discontinue.

Pulmonary toxicity: Discontinue treatment with pulmonary symptoms indicative of interstitial lung disease or pneumonitis which are ≥ grade 3

Other toxicities: Withhold for any toxicity (other than cardiac) ≥ grade 2 until toxicity resolves to ≤ grade 1 and reinitiate at the standard dose of 1,250 or 1,500 mg once daily; for persistent toxicity, reduce dosage

to 1,000 mg once daily (in combination with capecitabine) **or** 1,250 mg once daily (in combination with letrozole)

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Tablet, Oral:

Tykerb: 250 mg [contains fd&c yellow #6 (sunset yellow), fd&c yellow #6 aluminum lake]

Generic Equivalent Available (US) No

Prescribing and Access Restrictions Lapatinib is available through specialty pharmacies only. Information is available at www.gskcta.com or 1-866-265-6491.

Administration Administer once daily, on an empty stomach, 1 hour before or 1 hour after a meal. Take full dose at the same time each day; dividing dose throughout the day is not recommended.

Note: For combination treatment with capecitabine, capecitabine should be administered in 2 doses (approximately 12 hours apart) and taken with food or within 30 minutes after a meal.

Hazardous Drugs Handling Considerations

Hazardous agent (meets NIOSH 2016 criteria). This medication is not on the NIOSH (2016) list; however, it meets the criteria for a hazardous drug. Drugs are classified as hazardous based on their properties; the properties of a hazardous drug include one or more of the following characteristics: carcinogenic, teratogenic (or other developmental toxicity), reproductive toxicity, organotoxic at low doses, genotoxic, and/or new agents with structural or toxicity profiles similar to existing hazardous agents.

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends single gloving for administration of intact tablets or capsules. If manipulating tablets/capsules (eg, to prepare an oral suspension), NIOSH recommends double gloving, a protective gown, and preparation in a controlled device; if not prepared in a controlled device, respiratory and eye/face protection as well as ventilated engineering controls are recommended. NIOSH recommends double gloving, a protective gown, and (if there is a potential for vomit or spit up) eye/face protection for administration of an oral liquid/feeding tube administration (NIOSH 2016).

Use

Breast cancer: Treatment of human epidermal growth receptor type 2 (HER2) overexpressing advanced or metastatic breast cancer (in combination with capecitabine) in patients who have received prior therapy (with an anthracycline, a taxane, and trastuzumab); HER2 overexpressing hormone receptor–positive metastatic breast cancer in postmenopausal women where hormone therapy is indicated (in combination with letrozole)

Limitations of use: Patients should have disease progression on trastuzumab prior to initiation of

treatment with lapatinib in combination with capecitabine.

Use: Off-Label

HER2 overexpressing metastatic breast cancer (in combination with trastuzumab) with progression on prior trastuzumab-containing therapy; HER2 overexpressing metastatic breast cancer with brain metastases (in combination with capecitabine)

Medication Safety Issues

Sound-alike/look-alike issues:

Lapatinib may be confused with dasatinib, erlotinib, imatinib, lenvatinib, regorafenib, SUNItinib, vandetanib

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Adverse Reactions

Percentages reported for combination therapy.

>10%:

Central nervous system: Fatigue (≤20%), headache (14%)

Dermatologic: Palmar-plantar erythrodysesthesia (with capecitabine: 53%), skin rash (28% to 44%), alopecia (13%), xeroderma (10% to 13%), pruritus (12%), nail disease (11%)

Gastrointestinal: Diarrhea (64% to 65%), nausea (31% to 44%), vomiting (17% to 26%), mucositis (15%), stomatitis (14%), anorexia (11%), dyspepsia (11%)

Hematologic & oncologic: Decreased hemoglobin (with capecitabine: 56%; grade 3: <1%), decreased neutrophils (with capecitabine: 22%; grade 3: 3%; grade 4: <1%), decreased platelet count (with capecitabine: 18%; grade 3: <1%)

Hepatic: Increased serum AST (49% to 53%), increased serum ALT (37% to 46%), increased serum bilirubin (22% to 45%)

Neuromuscular & skeletal: Limb pain (12%), weakness (12%), back pain (11%)

Respiratory: Dyspnea (12%), epistaxis (11%)

1% to 10%:

Cardiovascular: Decreased left ventricular ejection fraction (with letrozole: 5%; with capecitabine: grade 2: 2%; grade 3: <1%)

Central nervous system: Insomnia (10%)

<1%, postmarketing, and/or case reports: Anaphylaxis, hepatotoxicity, hypersensitivity, interstitial

pulmonary disease, paronychia, pneumonitis, prolonged Q-T interval on ECG, severe dermatological reaction, Stevens-Johnson syndrome, torsades de pointes, toxic epidermal necrolysis, ventricular arrhythmia

Contraindications

Known severe hypersensitivity to lapatinib or any component of the formulation

Warnings/Precautions

Concerns related to adverse effects:

• Cardiotoxicity: Decreases in left ventricular ejection fraction (LVEF) have been reported (usually within the first 3 months of treatment); baseline and periodic LVEF evaluations are recommended. Interrupt treatment with decreased LVEF ≥ grade 2 or LVEF < LLN; may reinitiate with a reduced dose after a minimum of 2 weeks if the LVEF recovers and the patient is asymptomatic. Use with caution in conditions which may impair left ventricular function and in patients with a history of or predisposed to (prior treatment with anthracyclines, chest wall irradiation) left ventricular dysfunction. In a scientific statement from the American Heart Association, lapatinib has been determined to be an agent that may either cause reversible direct myocardial toxicity or exacerbate underlying myocardial dysfunction (magnitude: moderate/major) (AHA [Page 2016]).

• Dermatologic toxicity: Severe cutaneous reactions have been reported with use. Discontinue therapy if life-threatening dermatologic reactions (eg, progressive skin rash with blisters or mucosal lesions) such as erythema multiforme, Stevens-Johnson syndrome, or toxic epidermal necrolysis occur.

• Diarrhea: Diarrhea is common (onset is generally within 6 days and duration is 4 to 5 days); may be severe and/or fatal. Diarrhea is best managed with early intervention; instruct patients to immediately report any bowel pattern changes. After first unformed stool, administer antidiarrheal agents; severe diarrhea may require hydration, electrolytes, antibiotics (if duration >24 hours, fever, or grade 3/4 neutropenia), and/or treatment interruption, dose reduction, or discontinuation.

• Hepatotoxicity: **[US Boxed Warning]: Hepatotoxicity (ALT or AST >3 times ULN and total bilirubin >2 times ULN) has been reported with lapatinib; may be severe and/or fatal.** Onset may occur within days to several months after treatment initiation. Monitor transaminases, bilirubin, and alkaline phosphatase (at baseline and every 4 to 6 weeks during treatment, and as clinically indicated); discontinue with severe changes in liver function during treatment; do not reinitiate.

• Pulmonary toxicity: Interstitial lung disease (ILD) and pneumonitis have been reported (with lapatinib monotherapy and combination chemotherapy); monitor for pulmonary symptoms which may indicate ILD or pneumonitis; discontinue treatment for grade 3 (or higher) pulmonary symptoms indicative of ILD or pneumonitis (eg, dyspnea, dry cough).

• QTC prolongation: QTC prolongation has been observed; use caution in patients with a history of QTC prolongation or with medications known to prolong the QT interval; baseline and periodic 12-lead ECG should be considered; correct electrolyte (potassium, calcium, and magnesium) abnormalities prior to and during treatment. Concurrent use with other drugs which may prolong QTC interval may increase the risk of potentially fatal arrhythmias.

Disease related concerns:

• Hepatic impairment: Use with caution in patients with hepatic impairment; dose reductions should

be considered in patients with preexisting severe (Child-Pugh class C) hepatic impairment.

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Special populations:

• Pharmacogenomics: Patients who carry the HLA alleles DQA1*02:01 and DRB1*07:01 may experience a greater incidence of severe liver injury than patients who are noncarriers. These alleles are present in ~15% to 25% of Caucasian, Asian, African, and Hispanic patient populations and 1% in Japanese populations.

Metabolism/Transport Effects

Substrate of CYP3A4 (major), P-glycoprotein; **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential; **Inhibits** BCRP, CYP2C8 (moderate), CYP3A4 (weak), P-glycoprotein

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Afatinib: P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of Afatinib. Management: Per US labeling: reduce afatinib by 10mg if not tolerated. Per Canadian labeling: avoid combination if possible; if used, administer the P-gp inhibitor simultaneously with or after the dose of afatinib. *Risk D: Consider therapy modification*

Amodiaquine: CYP2C8 Inhibitors may increase the serum concentration of Amodiaquine. *Risk X: Avoid combination*

Aprepitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

ARIPiprazole: CYP3A4 Inhibitors (Weak) may increase the serum concentration of ARIPiprazole. Management: Monitor for increased aripiprazole pharmacologic effects. Aripiprazole dose adjustments may or may not be required based on concomitant therapy and/or indication. Consult full interaction monograph for specific recommendations. *Risk C: Monitor therapy*

Bilastine: P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of Bilastine. Management: Consider alternatives when possible; bilastine should be avoided in patients with moderate to severe renal insufficiency who are receiving p-glycoprotein inhibitors. *Risk D: Consider therapy modification*

Bosentan: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Brentuximab Vedotin: P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of Brentuximab Vedotin. Specifically, concentrations of the active monomethyl auristatin E (MMAE) component may be increased. *Risk C: Monitor therapy*

Colchicine: P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of Colchicine. Colchicine distribution into certain tissues (e.g., brain) may also be increased. Management: Colchicine is contraindicated in patients with impaired renal or hepatic function who are also receiving a p-

glycoprotein inhibitor. In those with normal renal and hepatic function, reduce colchicine dose as directed. *Risk D: Consider therapy modification*

Conivaptan: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

CYP2C8 Substrates: CYP2C8 Inhibitors (Moderate) may decrease the metabolism of CYP2C8 Substrates. *Risk C: Monitor therapy*

CYP3A4 Inducers (Moderate): May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

CYP3A4 Inducers (Strong): May decrease the serum concentration of Lapatinib. Management: If therapy overlap cannot be avoided, consider titrating lapatinib gradually from 1,250 mg/day up to 4,500 mg/day (HER2 positive metastatic breast cancer) or 1,500 mg/day up to 5,500 mg/day (hormone receptor/HER2 positive breast cancer) as tolerated. *Risk X: Avoid combination*

CYP3A4 Inhibitors (Moderate): May decrease the metabolism of CYP3A4 Substrates. *Risk C: Monitor therapy*

CYP3A4 Inhibitors (Strong): May increase the serum concentration of Lapatinib. Management: If an overlap in therapy cannot be avoided, consider reducing lapatinib adult dose to 500 mg/day during, and within 1 week of completing, treatment with the strong CYP3A4 inhibitor. *Risk X: Avoid combination*

Dabigatran Etexilate: P-glycoprotein/ABCB1 Inhibitors may increase serum concentrations of the active metabolite(s) of Dabigatran Etexilate. Management: Dabigatran dose reductions may be needed. Specific recommendations vary considerably according to US vs Canadian labeling, specific P-gp inhibitor, renal function, and indication for dabigatran treatment. Refer to full monograph or dabigatran labeling. *Risk D: Consider therapy modification*

Dabrafenib: May decrease the serum concentration of CYP3A4 Substrates. Management: Seek alternatives to the CYP3A4 substrate when possible. If concomitant therapy cannot be avoided, monitor clinical effects of the substrate closely (particularly therapeutic effects). *Risk D: Consider therapy modification*

Dasatinib: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Deferasirox: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Dexamethasone (Systemic): May decrease the serum concentration of Lapatinib. Management: If therapy overlap cannot be avoided, consider titrating lapatinib gradually from 1,250 mg/day up to 4,500 mg/day (HER2 positive metastatic breast cancer) or 1,500 mg/day up to 5,500 mg/day (hormone receptor/HER2 positive breast cancer) as tolerated. *Risk X: Avoid combination*

DOXOrubicin (Conventional): P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of DOXOrubicin (Conventional). Management: Seek alternatives to P-glycoprotein inhibitors in patients treated with doxorubicin whenever possible. One U.S. manufacturer (Pfizer Inc.) recommends that these combinations be avoided. *Risk D: Consider therapy modification*

Edoxaban: P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of Edoxaban. Management: See full monograph for details. Reduced doses are recommended for patients receiving edoxaban for venous thromboembolism in combination with certain inhibitors. Similar dose adjustment is not recommended for edoxaban use in atrial fibrillation. *Risk D: Consider therapy modification*

Everolimus: P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of Everolimus. Management: Everolimus dose reductions are required for patients being treated for subependymal giant cell astrocytoma or renal cell carcinoma. See prescribing information for specific dose adjustment and monitoring recommendations. *Risk D: Consider therapy modification*

Flibanserin: CYP3A4 Inhibitors (Weak) may increase the serum concentration of Flibanserin. *Risk C: Monitor therapy*

Fosaprepitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Fusidic Acid (Systemic): May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

Grapefruit Juice: May increase the serum concentration of Lapatinib. *Risk X: Avoid combination*

Highest Risk QTc-Prolonging Agents: QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying) may enhance the QTc-prolonging effect of Highest Risk QTc-Prolonging Agents. Management: Avoid such combinations when possible. Use should be accompanied by close monitoring for evidence of QT prolongation or other alterations of cardiac rhythm. *Risk D: Consider therapy modification*

HYDROcodone: CYP3A4 Inhibitors (Weak) may increase the serum concentration of HYDROcodone. *Risk C: Monitor therapy*

Idelalisib: May increase the serum concentration of CYP3A4 Substrates. *Risk X: Avoid combination*

Lomitapide: CYP3A4 Inhibitors (Weak) may increase the serum concentration of Lomitapide. Management: Patients on lomitapide 5 mg/day may continue that dose. Patients taking lomitapide 10 mg/day or more should decrease the lomitapide dose by half. The lomitapide dose may then be titrated up to a max adult dose of 30 mg/day. *Risk D: Consider therapy modification*

Moderate Risk QTc-Prolonging Agents: QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying) may enhance the QTc-prolonging effect of Moderate Risk QTc-Prolonging Agents. *Risk C: Monitor therapy*

Naldemedine: P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of Naldemedine. *Risk C: Monitor therapy*

Naloxegol: P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of Naloxegol. *Risk C: Monitor therapy*

Netupitant: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

NiMODipine: CYP3A4 Inhibitors (Weak) may increase the serum concentration of NiMODipine. *Risk C: Monitor therapy*

Palbociclib: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

PAZOPanib: Lapatinib may enhance the QTc-prolonging effect of PAZOPanib. Lapatinib may increase the serum concentration of PAZOPanib. *Risk X: Avoid combination*

P-glycoprotein/ABCB1 Inhibitors: May increase the serum concentration of P-glycoprotein/ABCB1 Substrates. P-glycoprotein inhibitors may also enhance the distribution of p-glycoprotein substrates to specific cells/tissues/organs where p-glycoprotein is present in large amounts (e.g., brain, T-lymphocytes, testes, etc.). *Risk C: Monitor therapy*

P-glycoprotein/ABCB1 Substrates: P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of P-glycoprotein/ABCB1 Substrates. P-glycoprotein inhibitors may also enhance the distribution of p-glycoprotein substrates to specific cells/tissues/organs where p-glycoprotein is present in large amounts (e.g., brain, T-lymphocytes, testes, etc.). *Risk C: Monitor therapy*

Pimozide: CYP3A4 Inhibitors (Weak) may increase the serum concentration of Pimozide. *Risk X: Avoid combination*

Prucalopride: P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of Prucalopride. *Risk C: Monitor therapy*

Ranolazine: P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of Ranolazine. *Risk C: Monitor therapy*

Ranolazine: May increase the serum concentration of P-glycoprotein/ABCB1 Substrates. *Risk C: Monitor therapy*

RifAXIMin: P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of RifAXIMin. *Risk C: Monitor therapy*

Sarilumab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Silodosin: P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of Silodosin. *Risk X: Avoid combination*

Siltuximab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Simeprevir: May increase the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

St John's Wort: May decrease the serum concentration of Lapatinib. Management: If therapy overlap cannot be avoided, consider titrating lapatinib gradually from 1,250 mg/day up to 4,500 mg/day (HER2 positive metastatic breast cancer) or 1,500 mg/day up to 5,500 mg/day (hormone receptor/HER2 positive breast cancer) as tolerated. *Risk X: Avoid combination*

Stiripentol: May increase the serum concentration of CYP3A4 Substrates. Management: Use of stiripentol with CYP3A4 substrates that are considered to have a narrow therapeutic index should be avoided due to the increased risk for adverse effects and toxicity. Any CYP3A4 substrate used with stiripentol requires closer monitoring. *Risk D: Consider therapy modification*

Tocilizumab: May decrease the serum concentration of CYP3A4 Substrates. *Risk C: Monitor therapy*

Topotecan: P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of Topotecan. *Risk X: Avoid combination*

Venetoclax: P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of Venetoclax. Management: Reduce the venetoclax dose by at least 50% in patients requiring these combinations. *Risk D: Consider therapy modification*

VinCRIStine (Liposomal): P-glycoprotein/ABCB1 Inhibitors may increase the serum concentration of VinCRIStine (Liposomal). *Risk X: Avoid combination*

Food Interactions Systemic exposure of lapatinib is increased when administered with food (AUC three- to fourfold higher). Grapefruit juice may increase the levels/effects of lapatinib. Management:

Administer once daily on an empty stomach, 1 hour before or 1 hour after a meal at the same time each day. Avoid grapefruit juice. Maintain adequate hydration, unless instructed to restrict fluid intake.

Pregnancy Risk Factor

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Pregnancy Implications

Adverse events were demonstrated in animal reproduction studies. Lapatinib may cause fetal harm if administered during pregnancy. Women of childbearing potential should be advised to avoid pregnancy during treatment.

European Society for Medical Oncology (ESMO) guidelines for cancer during pregnancy recommend delaying treatment with HER-2 targeted agents until after delivery in pregnant patients with HER-2 positive disease (Peccatori 2013).

Breast-Feeding Considerations

It is not known if lapatinib is excreted in breast milk. Due to the potential for serious adverse reactions in the nursing infant, the decision to discontinue lapatinib or discontinue breast-feeding during treatment should take in account the benefits of treatment to the mother.

Dietary Considerations

Avoid grapefruit juice.

Monitoring Parameters

LVEF (baseline and periodic), CBC with differential, liver function tests, including transaminases, bilirubin, and alkaline phosphatase (baseline and every 4-6 weeks during treatment); electrolytes including calcium, potassium, magnesium; monitor for fluid retention; ECG monitoring if at risk for QTc prolongation; symptoms of ILD or pneumonitis; monitor for diarrhea and dermatologic toxicity

Mechanism of Action

Tyrosine kinase (dual kinase) inhibitor; inhibits EGFR (ErbB1) and HER2 (ErbB2) by reversibly binding to tyrosine kinase, blocking phosphorylation and activation of downstream second messengers (Erk1/2 and Akt), regulating cellular proliferation and survival in ErbB- and ErbB2-expressing tumors. Combination therapy with lapatinib and endocrine therapy may overcome endocrine resistance occurring in HER2+ and hormone receptor positive disease.

Pharmacodynamics/Kinetics

Absorption: Incomplete and variable

Protein binding: >99% to albumin and $alpha_1$-acid glycoprotein

Metabolism: Hepatic; extensive via CYP3A4 and 3A5, and to a lesser extent via CYP2C19 and 2C8 to oxidized metabolites

Half-life elimination: ~24 hours

Time to peak, plasma: ~4 hours (Burris 2009)

Excretion: Feces (27% as unchanged drug; range 3% to 67%); urine (<2%)

Pricing: US

Tablets (Tykerb Oral)

250 mg (150): $8156.12

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of

the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names Tayverb (UA); Tykerb (AE, AR, AU, BH, BR, CL, CO, CR, DO, HK, HN, ID, IL, IN, JO, JP, KR, KW, LB, LK, MY, NZ, PA, PE, PH, QA, SA, SG, SV, TH, TW, UY); Tyverb (AT, BE, CH, CY, CZ, DE, DK, EE, ES, FR, GB, GR, HR, IE, IS, IT, LT, LU, LV, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR)

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