Capecitabine: Drug information

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

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

ALERT: US Boxed Warning

Warfarin interaction:

Frequently monitor the anticoagulant response (international normalized ratio [INR] or prothrombin time [PT]) of patients receiving concomitant capecitabine and oral coumarin-derivative anticoagulant therapy in order to adjust the anticoagulant dose accordingly. A clinically important capecitabine-warfarin drug interaction was demonstrated in a clinical pharmacology trial. Altered coagulation parameters and/or bleeding, including death, have been reported in patients taking capecitabine concomitantly with coumarin-derivative anticoagulants such as warfarin and phenprocoumon. Postmarketing reports have shown clinically significant increases in PT and INR in patients who were stabilized on anticoagulants at the time capecitabine was introduced. These events occurred within several days and up to several months after initiating capecitabine therapy and, in a few cases, within 1 month after stopping capecitabine. These events occurred in patients with and without liver metastases. Age older than 60 years and a diagnosis of cancer independently predispose patients to an increased risk of coagulopathy.

Brand Names: US

Xeloda

Brand Names: Canada

Teva-Capecitabine; Xeloda

Pharmacologic Category

Antineoplastic Agent, Antimetabolite; Antineoplastic Agent, Antimetabolite (Pyrimidine Analog)

Dosing: Adult

Breast cancer, metastatic: Oral: 1,250 mg/m^2 twice daily for 2 weeks, every 21 days (as either monotherapy or in combination with docetaxel)

Breast cancer, metastatic (off-label dosing): Oral: 1,000 mg/m^2 twice daily (in combination with ixabepilone) on days 1 to 14 of a 3-week cycle until disease progression or unacceptable toxicity (Thomas 2007)

Breast cancer, metastatic, HER2+ (off-label dosing): Oral: 1,000 mg/m^2 twice daily (in combination with lapatinib) on days 1 to 14 of a 3-week cycle until disease progression or unacceptable toxicity (Geyer 2006) or 1,250 mg/m^2 twice daily (in combination with trastuzumab) on days 1 to 14 of a 3-week cycle (Bartsch 2007)

Breast cancer, metastatic, HER2+ with brain metastases, first-line therapy (off-label dosing): Oral:

1,000 mg/m2 twice daily (in combination with lapatinib) on days 1 to 14 of a 3-week cycle until disease progression or unacceptable toxicity (Bachelot 2012)

Colorectal cancer, metastatic: Oral: 1,250 mg/m^2 twice daily for 2 weeks, every 21 days. **Note:** Capecitabine toxicities, particularly hand-foot syndrome, may be higher in North American populations; therapy initiation at doses of 1,000 mg/m^2 twice daily (for 2 weeks every 21 days) may be considered (Haller 2008).

Colorectal cancer (off-label combination): Oral: 1,000 mg/m^2 twice daily (in combination with oxaliplatin) on days 1 to 14 of a 3-week cycle for 8 or 16 cycles (Cassidy 2008; Haller 2011; Schmoll 2007)

Dukes' C colon cancer, adjuvant therapy: Oral: 1,250 mg/m^2 twice daily for 2 weeks, every 21 days, for a recommended total duration of 24 weeks (8 cycles of 2 weeks of drug administration and 1 week rest period).

Anal carcinoma (off-label use): Oral: 825 mg/m^2 twice daily 5 days/week (Monday through Friday) (in combination with mitomycin [on day 1 only]) during radiation therapy; radiation therapy occurred over 5 to 6 weeks (Oliveria 2016) **or** 825 mg/m^2 twice daily on radiation therapy days (in combination with mitomycin [on day 1 only] and radiation therapy) (Meulendijks 2014; Thind 2014)

Esophageal and gastric cancers (off-label uses): Oral:

Preoperative or definitive chemoradiation: 800 mg/m^2 twice daily (in combination with cisplatin and radiation) on days 1 to 5 weekly for 5 weeks (Lee 2007) **or** 625 mg/m^2 twice daily (in combination with oxaliplatin and radiation) on days 1 to 5 weekly for 5 weeks (Javle 2009)

Postoperative chemoradiation: 625 to 825 mg/m^2 twice daily during radiation therapy (Lee 2006)

Locally advanced or metastatic (chemoradiation not indicated): 1,000 to 1,250 mg/m^2 twice daily (monotherapy or in combination with cisplatin with or without trastuzumab) on days 1 to 14 of a 3-week cycle (Bang 2010; Hong 2004; Kang 2009) **or** 625 mg/m^2 twice daily (in combination with epirubicin and cisplatin or oxaliplatin) on days 1 to 21 of a 3-week cycle for up to 8 cycles (Cunningham 2008; Sumpter 2005)

Hepatobiliary cancers, advanced (off-label use): Oral: 650 mg/m^2 twice daily (in combination with gemcitabine) on days 1 to 14 of a 3-week cycle (Knox 2005) **or** 1,000 mg/m^2 twice daily (in combination with oxaliplatin) on days 1 to 14 of a 3-week cycle (Nehls 2008) **or** 1,250 mg/m^2 twice daily (in combination with cisplatin) on days 1 to 14 of a 3-week cycle (Kim 2003); all regimens continued until disease progression or unacceptable toxicity

Neuroendocrine (pancreatic/islet cell) tumors, metastatic or unresectable (off label use): Oral: 750 mg/m^2 twice daily (in combination with temozolomide) on days 1 to 14 of a 4-week cycle (Strosberg 2011)

Ovarian, fallopian tube, or peritoneal cancer, platinum-refractory (off label use): Oral: 1,000 mg/m^2 twice daily on days 1 to 14 of a 3-week cycle until disease progression or unacceptable toxicity (Wolf 2006)

Pancreatic cancer (adjuvant therapy) (off-label use): Oral: 1,660 mg/m^2/**day** (in 2 divided doses) days 1 to 21 every 28 days (in combination with gemcitabine) for 6 cycles beginning within 12 weeks of resection (Neoptolemos 2017). American Society of Clinical Oncology guidelines recommend initiating within 8 weeks of resection (ASCO [Khorana 2017]).

Pancreatic cancer, metastatic (off-label use): Oral: 1,250 mg/m^2 twice daily on days 1 to 14 of a 3-week cycle (Cartwright 2002) **or** 830 mg/m^2 twice daily (in combination with gemcitabine) on days 1 to 21 of a 4-week cycle until disease progression or unacceptable toxicity (Cunningham 2009)

Unknown primary cancer (off-label use): Oral: 1,000 mg/m^2 twice daily (in combination with oxaliplatin) on days 1 to 14 of a 3-week cycle for up to 6 cycles or until disease progression (Hainsworth 2010) **or** 800 mg/m^2 twice daily (in combination with carboplatin and gemcitabine) on days 1 to 14 of a 3-week cycle for up to 8 cycles or until disease progression or unacceptable toxicity (Schneider 2007)

Dosing: Geriatric

The elderly may be more sensitive to the toxic effects of fluorouracil. Insufficient data are available to provide dosage modifications.

Dosing: Renal Impairment

Note: Renal function may be estimated using the Cockcroft-Gault formula for dosage adjustment purposes.

Renal impairment at treatment initiation:

CrCl ≥51 mL/minute: Initial: No dosage adjustment necessary.

CrCl 30 to 50 mL/minute: Initial: Reduce dose to 75% of usual dose (Cassidy 2002; Poole 2002; Xeloda prescribing information 2016)

CrCl <30 mL/minute: Use is contraindicated (Poole 2002; Xeloda prescribing information 2016)

Renal toxicity during treatment: Refer to dosage adjustment for toxicity.

Dosing: Hepatic Impairment

Hepatic impairment at treatment initiation:

Mild to moderate impairment: No starting dose adjustment necessary (Ecklund 2005; Superfin 2007); however, carefully monitor patients.

Severe hepatic impairment: There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Hepatotoxicity during treatment: Hyperbilirubinemia, grade 3 or 4: Interrupt treatment until bilirubin ≤3 times ULN; refer to dosage adjustment for toxicity for dosage recommendations.

Dosing: Obesity

ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer: Utilize patient's actual body weight (full weight) for calculation of body surface area- or weight-based dosing, particularly when the intent of therapy is curative; manage regimen-related toxicities in the same manner as for nonobese patients; if a dose reduction is utilized due to toxicity, consider resumption of full weight-based dosing with subsequent cycles, especially if cause of toxicity (eg, hepatic or renal impairment) is resolved (Griggs 2012). The manufacturer recommends capping the dose (at a maximum of 5,600 mg/day) in patients with a body surface area of 2.18 m^2 or higher (refer to product labeling for details).

Dosing: Adjustment for Toxicity

See table (**Note:** Capecitabine dosing recommendations apply to both monotherapy and when used in combination therapy with docetaxel).

Monitor carefully for toxicity and adjust dose as necessary. Doses reduced for toxicity should not be increased at a later time. For combination therapy, also refer to docetaxel product labeling for docetaxel dose modifications. If treatment delay is required for either capecitabine or docetaxel, withhold both agents until appropriate to resume combination treatment.

Recommended Capecitabine Dose Modifications

Toxicity Grades	During a Course of Therapy	Dose Adjustment for Next Cycle (% of starting dose)
Grade 1	Maintain dose level	Maintain dose level
Grade 2		
1st appearance	Interrupt until resolved to grade 0 to 1	100%
2nd appearance	Interrupt until resolved to grade 0 to 1	75%
3rd appearance	Interrupt until resolved to grade 0 to 1	50%
4th appearance	Discontinue treatment permanently	
Grade 3		
1st appearance	Interrupt until resolved to grade 0 to 1	75%
2nd appearance	Interrupt until resolved to grade 0 to 1	50%
3rd appearance	Discontinue treatment permanently	
Grade 4		
1st appearance	Discontinue permanently	
	or	

	If in the patient's best interest to continue, interrupt until resolved to grade 0 to 1	50%

Dosage adjustments for hematologic toxicity in combination therapy with ixabepilone:

Neutrophils <500/mm^3 for ≥7 days or neutropenic fever: Hold for concurrent diarrhea or stomatitis until neutrophils recover to >1000/mm^3, then continue at same dose

Platelets <25,000/mm^3 (or <50,000/mm^3 with bleeding): Hold for concurrent diarrhea or stomatitis until platelets recover to >50,000/mm^3, then continue at same dose

Dosage Forms

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

Tablet, Oral:

Xeloda: 150 mg, 500 mg

Generic: 150 mg, 500 mg

Generic Equivalent Available (US)

Yes

Administration

Usually administered in 2 divided doses taken 12 hours apart. Doses should be taken with water within 30 minutes after a meal. Swallow tablets whole. Avoid cutting or crushing tablets.

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

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, metastatic:

Monotherapy: Treatment of metastatic breast cancer resistant to both paclitaxel and an anthracycline-containing regimen or resistant to paclitaxel in patients for whom further anthracycline therapy is not indicated

Combination therapy: Treatment of metastatic breast cancer (in combination with docetaxel) after failure of a prior anthracycline-containing regimen

Colorectal cancer: First-line treatment of metastatic colorectal cancer when treatment with a fluoropyrimidine alone is preferred; adjuvant therapy of Dukes' C colon cancer after complete resection of the primary tumor when fluoropyrimidine therapy alone is preferred

Use: Off-Label

Anal carcinoma; Esophageal and gastric cancers; Hepatobiliary cancers, advanced; Neuroendocrine (islet cell) tumors, metastatic or unresectable; Ovarian, fallopian tube, or peritoneal cancers, refractory; Pancreatic cancer (adjuvant therapy); Pancreatic cancer (locally advanced or metastatic); Unknown primary cancer

Medication Safety Issues

Sound-alike/look-alike issues:

Xeloda may be confused with Xenical

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

Frequency listed derived from monotherapy trials. Incidence reported for all indications and usage, unless otherwise noted. Frequency not always defined.

>10%:

Cardiovascular: Edema (≤15%)

Central nervous system: Fatigue (≤42%), paresthesia (stage IV breast cancer: 21%; grades 3/4: 1%), pain (≤12%)

Dermatologic: Palmar-plantar erythrodysesthesia (54% to 60%; grades ≥3: 11% to 17%), dermatitis (27% to 37%, grades ≥3: 1%)

Gastrointestinal: Diarrhea (47% to 57%, grades 3/4: 2% to 13%), nausea (34% to 43%; stage IV breast cancer: 53%), vomiting (metastatic colorectal cancer, stage IV breast cancer: 27% to 37%; Dukes' C colon cancer: 15%), abdominal pain (metastatic colorectal cancer: 35%; stage IV breast cancer: 20%; Dukes' C colon cancer: 14%), decreased appetite (26%), stomatitis (22% to 25%), anorexia (stage IV breast cancer: 23%; Dukes' C colon cancer: 9%), constipation (9% to 15%)

Hematologic & oncologic: Lymphocytopenia (stage IV breast cancer: 94%; stage IV breast cancer, grades 3/4: 15% to 44%), anemia (72% to 80%, grades 3/4: ≤3%), neutropenia (≤26%, grades 3/4: ≤3%), thrombocytopenia (stage IV breast cancer: 24%; all: grades 3/4: 1% to 3%)

Hepatic: Hyperbilirubinemia (Metastatic colorectal cancer: 48%; stage IV breast cancer: 22%; all: grades 3/4: 2% to 23%)

Neuromuscular & skeletal: Weakness (≤42%)

Ophthalmic: Eye irritation (13% to 15%)

Miscellaneous: Fever (7% to 18%)

1% to 10%:

Cardiovascular: Venous thrombosis (8%), chest pain (≤6%), atrial fibrillation (<5%), bradycardia (<5%), collapse (<5%), extrasystoles (<5%), pericardial effusion (<5%), ventricular premature contractions (<5%), angina pectoris, cardiac arrest, cardiac arrhythmia, cardiac failure, cardiomyopathy, ECG changes, ischemic heart disease, myocardial infarction

Central nervous system: Lethargy (10%), peripheral sensory neuropathy (10%), headache (5% to 10%), insomnia (≤8%), dizziness (6% to 8%), ataxia (<5%), depression (≤5%), mood changes (5%), abnormal gait (<5%), brain disease (<5%), dysarthria (<5%), dysphasia (<5%), equilibrium disturbance (<5%), irritability (<5%), myasthenia (<5%), sedation (<5%), vertigo (<5%)

Dermatologic: Nail disease (≤7%), skin discoloration (7%), skin rash (7%), alopecia (6%), erythema (6%), dermal ulcer (<5%), pruritus (<5%)

Endocrine & metabolic: Dehydration (7%), hot flash (<5%), hypokalemia (<5%), hypomagnesemia (<5%), increased thirst (<5%), weight gain (<5%), decreased serum calcium (Dukes' C colon cancer: grades 3/4: 2%), increased serum calcium (Dukes' C colon cancer: grades 3/4: 1%)

Gastrointestinal: Gastrointestinal motility disorder (10%), GI inflammation (upper: 8%), oral discomfort (grades 3/4: 10%), dyspepsia (6% to 8%), upper abdominal pain (7%), intestinal obstruction (≤6%), dysgeusia (6%), gastrointestinal hemorrhage (6%), abdominal distention (<5%), dysphagia (<5%), rectal pain (<5%), toxic dilation of intestine (<5%), sore throat (2%), necrotizing enterocolitis

Hematologic & oncologic: Hemorrhage (<5%), lymphedema (<5%), granulocytopenia (Dukes' C colon cancer: grades 3/4: 3%), immune thrombocytopenia (1%)

Hepatic: Abnormal hepatic function tests (<5%), increased serum ALT (Dukes' C colon cancer: grades 3/4: 2%)

Hypersensitivity: Drug-induced hypersensitivity (<5%)

Infection: Viral infection (metastatic colorectal cancer: 5%)

Neuromuscular & skeletal: Back pain (10%), myalgia (≤9%), arthralgia (8%), limb pain (stage IV breast cancer: 6%), tremor (<5%)

Ophthalmic: Visual disturbance (metastatic colorectal cancer: 5%), conjunctivitis (≤5%), keratoconjunctivitis (<5%)

Respiratory: Cough (≤7%), chest mass (<5%), dyspnea (<5%), flu-like symptoms (<5%), hemoptysis (<5%), hoarseness (<5%), pharyngeal disease (metastatic colorectal cancer: 5%), epistaxis (≤3%), laryngitis (1%)

<1%, postmarketing, and/or case reports (limited to important or life-threatening): Acute renal failure, arthritis, ascites, asthma, blood coagulation disorder, bone marrow depression, bronchitis, bronchopneumonia, bronchospasm, cachexia, cerebrovascular accident, cholestatic hepatitis, confusion, cutaneous lupus erythematosus, diaphoresis, ecchymoses, esophagitis, fibrosis, flu-like symptoms, fungal infection, gastric ulcer, gastroenteritis, gastrointestinal perforation, hepatic failure, hepatic fibrosis, hepatitis, hypersensitivity, hypertension, hypertriglyceridemia, hypotension, jaundice, keratitis, lacrimal

stenosis, leukoencephalopathy, leukopenia, loss of consciousness, myocarditis, nocturia, ostealgia, pancytopenia, phlebitis (venous), photophobia, pneumonia, pulmonary embolism, radiation recall phenomenon, renal insufficiency, respiratory distress, sepsis, Stevens-Johnson syndrome, syncope, tachycardia, toxic epidermal necrolysis

Contraindications

Known hypersensitivity to capecitabine, fluorouracil, or any component of the formulation; severe renal impairment (CrCl <30 mL/minute)

Canadian labeling: Additional contraindications (not in the US labeling): Known complete absence of dihydropyrimidine dehydrogenase (DPD) activity; concomitant administration with sorivudine or chemically related analogues (eg, brivudine)

Warnings/Precautions

Concerns related to adverse effects:

• Bone marrow suppression: Bone marrow suppression may occur, hematologic toxicity is more common when used in combination therapy; use with caution; dosage adjustments may be required. The product labeling recommends that patients with baseline platelets <100,000/mm^3 and/or neutrophils <1,500/mm^3 not receive capecitabine therapy and also to withhold therapy for grade 3 or 4 hematologic toxicity during treatment.

• Cardiotoxicity: Cardiotoxicity has been observed with capecitabine, including myocardial infarction, ischemia, angina, dysrhythmias, cardiac arrest, cardiac failure, sudden death, ECG changes, and cardiomyopathy. These adverse events may be more common in patients with a history of coronary artery disease. In a scientific statement from the American Heart Association, capecitabine 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: Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN) have been reported (some fatal); permanently discontinue capecitabine if a severe dermatologic or mucocutaneous reaction occurs.

• Gastrointestinal toxicity: May cause diarrhea (may be severe); median time to first occurrence of grade 2 to 4 diarrhea was 34 days and median duration of grades 3 or 4 diarrhea was 5 days. Withhold treatment for grades 2 to 4 diarrhea; subsequent doses should be reduced after grade 3 or 4 diarrhea or recurrence of grade 2 diarrhea. Antidiarrheal therapy (eg, loperamide) is recommended. Dehydration may occur rapidly in patients with diarrhea, nausea, vomiting, anorexia, and/or weakness; adequately hydrate prior to treatment initiation. Elderly patients may be at higher risk for dehydration. Interrupt treatment for grade 2 or higher dehydration; correct precipitating factors and ensure rehydration prior to resuming therapy; may require dose modification (based on precipitating factor). Necrotizing enterocolitis (typhlitis) has been reported.

• Hand-and-foot syndrome: May cause hand-and-foot syndrome (palmar-plantar erythrodysesthesia or chemotherapy-induced acral erythema); characterized by numbness, dysesthesia/paresthesia, tingling, painless or painful swelling, erythema, desquamation, blistering, and severe pain. The median onset is 79 days (range: 11 to 360 days). Persistent hand-and-foot syndrome (grade 2 and higher) could eventually lead to fingerprint loss. If grade 2 or 3 hand-and-foot syndrome occurs,

interrupt administration of capecitabine until the event resolves or decreases in intensity to grade 1. Following grade 3 hand-and-foot syndrome, decrease subsequent doses of therapy.

• Hepatotoxicity: Grade 3 and 4 hyperbilirubinemia have been observed in patients with and without hepatic metastases at baseline (median onset: 64 days). Transaminase and alkaline phosphatase elevations have also been reported. If capecitabine-related grade 3 or 4 hyperbilirubinemia occurs, interrupt treatment until bilirubin ≤3 times ULN. Bilirubin elevations may also require dose reductions.

Disease-related concerns:

• Dihydropyrimidine dehydrogenase deficiency: Patients with certain homozygous or heterozygous mutations of the dihydropyrimidine dehydrogenase (DPD) enzyme are at increased risk for acute early-onset (potentially severe, life-threatening, or fatal) toxicity due to total or near total absence of DPD activity. Toxicity may include mucositis/stomatitis, diarrhea, neutropenia, and neurotoxicity. Patients with partial DPD activity are also at risk for severe, life-threatening, or fatal toxicity. May require therapy interruption or permanent discontinuation, depending on the onset, duration, and severity of toxicity observed. No capecitabine dose has been shown to be safe in patients with complete DPD deficiency; data is insufficient to recommend a dose in patients with partial DPD activity.

• Hepatic impairment: Use with caution in patients with mild to moderate hepatic impairment due to liver metastases. The effect of severe hepatic impairment has not been studied.

• Renal impairment: Dehydration may occur, resulting in acute renal failure (may be fatal); concomitant use with nephrotoxic agents and baseline renal dysfunction may increase the risk. Use with caution in patients with mild to moderate renal impairment; reduce dose with moderate impairment (exposure to capecitabine and metabolites is increased) and carefully monitor and reduce subsequent dose (with any grade 2 or higher adverse effect) with mild to moderate impairment. Use is contraindicated in severe 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.

• Fluorouracil/leucovorin (FU/LV): In patients with colorectal cancer, treatment with capecitabine immediately following 6 weeks of FU/LV therapy has been associated with an increased incidence of grade ≥3 toxicity, when compared to patients receiving the reverse sequence, capecitabine (two 3-week courses) followed by FU/LV (Hennig 2008).

• Warfarin: **[US Boxed Warning]: Capecitabine may increase the anticoagulant effects of warfarin; bleeding events, including death, have occurred with concomitant use. Clinically significant increases in prothrombin time (PT) and INR have occurred within several days to months after capecitabine initiation (in patients previously stabilized on anticoagulants), and may continue up to 1 month after capecitabine discontinuation. May occur in patients with or without liver metastases. Monitor PT and INR frequently and adjust anticoagulation dosing accordingly. An increased risk of coagulopathy is correlated with a cancer diagnosis and age >60 years.**

Special populations:

• Elderly: Use with caution in patients ≥60 years of age; the incidence of treatment-related adverse events may be higher.

Other warnings/precautions:

• Fluoropyrimidine overdose: Uridine triacetate (formerly called vistonuridine), has been studied in cases of fluoropyrimidine overdose. In a clinical study of 98 patients who received uridine triacetate for fluorouracil toxicity (due to overdose, accidental capecitabine ingestion, or possible DPD deficiency), 96 patients recovered fully (Bamat 2013). Of 17 patients receiving uridine triacetate beginning within 8 to 96 hours after fluorouracil overdose, all patients fully recovered (von Borstel 2009). An additional case report describes accidental capecitabine ingestion by a 22-month-old child; uridine triacetate was initiated approximately 7 hours after exposure. The patient received uridine triacetate every 6 hours for a total of 20 doses through nasogastric tube administration; he was asymptomatic throughout his course and was discharged with normal laboratory values (Kanie 2011). Refer to Uridine Triacetate monograph.

Metabolism/Transport Effects **Inhibits** CYP2C9 (strong)

Drug Interactions

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

Alitretinoin (Systemic): CYP2C9 Inhibitors (Strong) may increase the serum concentration of Alitretinoin (Systemic). Management: Consider reducing the alitretinoin dose to 10 mg when used together with strong CYP2C9 inhibitors. Monitor for increased alitretinoin effects/toxicities if combined with a strong CYP2C9 inhibitor. *Risk D: Consider therapy modification*

BCG (Intravesical): Immunosuppressants may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

BCG (Intravesical): Myelosuppressive Agents may diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

Bosentan: CYP2C9 Inhibitors (Strong) may increase the serum concentration of Bosentan. Management: Concomitant use of both a CYP2C9 inhibitor and a CYP3A inhibitor or a single agent that inhibits both enzymes with bosentan is likely to cause a large increase in serum concentrations of bosentan and is not recommended. See monograph for details. *Risk C: Monitor therapy*

Cannabis: CYP2C9 Inhibitors (Strong) may increase the serum concentration of Cannabis. More specifically, tetrahydrocannabinol serum concentrations may be increased. *Risk C: Monitor therapy*

Carvedilol: CYP2C9 Inhibitors (Strong) may increase the serum concentration of Carvedilol. Specifically, concentrations of the S-carvedilol enantiomer may be increased. *Risk C: Monitor therapy*

Cimetidine: May increase serum concentrations of the active metabolite(s) of Capecitabine. Specifically, concentrations of fluorouracil may be increased. *Risk C: Monitor therapy*

CloZAPine: Myelosuppressive Agents may enhance the adverse/toxic effect of CloZAPine. Specifically, the risk for neutropenia may be increased. *Risk C: Monitor therapy*

Coccidioides immitis Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioides immitis Skin Test. *Risk C: Monitor therapy*

CYP2C9 Substrates: CYP2C9 Inhibitors (Strong) may decrease the metabolism of CYP2C9 Substrates. *Risk D: Consider therapy modification*

Deferiprone: Myelosuppressive Agents may enhance the neutropenic effect of Deferiprone. *Risk X: Avoid combination*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor therapy*

Diclofenac (Systemic): CYP2C9 Inhibitors (Strong) may increase the serum concentration of Diclofenac (Systemic). Management: Consider using a lower dose of diclofenac when used together with a strong CYP2C9 inhibitor. Arthrotec (diclofenac and misoprostol) labeling specifically recommends limiting the total daily dose to a maximum of 50 mg twice/day. *Risk D: Consider therapy modification*

Dipyrone: May enhance the adverse/toxic effect of Myelosuppressive Agents. Specifically, the risk for agranulocytosis and pancytopenia may be increased *Risk X: Avoid combination*

Dronabinol: CYP2C9 Inhibitors (Strong) may increase the serum concentration of Dronabinol. *Risk C: Monitor therapy*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Fingolimod: Immunosuppressants may enhance the immunosuppressive effect of Fingolimod. Management: Avoid the concomitant use of fingolimod and other immunosuppressants when possible. If combined, monitor patients closely for additive immunosuppressant effects (eg, infections). *Risk D: Consider therapy modification*

Fosphenytoin: Capecitabine may increase the serum concentration of Fosphenytoin. *Risk D: Consider therapy modification*

Gimeracil: May increase serum concentrations of the active metabolite(s) of Capecitabine. Specifically, gimeracil may increase concentrations of fluorouracil. *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*

Lacosamide: CYP2C9 Inhibitors (Strong) may increase the serum concentration of Lacosamide. *Risk C: Monitor therapy*

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

Lenograstim: Antineoplastic Agents may diminish the therapeutic effect of Lenograstim. *Risk D: Consider therapy modification*

Leucovorin Calcium-Levoleucovorin: May enhance the adverse/toxic effect of Capecitabine. *Risk C: Monitor therapy*

MetroNIDAZOLE (Systemic): May increase serum concentrations of the active metabolite(s) of Capecitabine. *Risk C: Monitor therapy*

MiFEPRIStone: May enhance the QTc-prolonging effect of QTc-Prolonging Agents (Indeterminate Risk and Risk Modifying). Management: Though the drugs listed here have uncertain QT-prolonging effects, they all have some possible association with QT prolongation and should generally be avoided when possible. *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*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Nivolumab: Immunosuppressants may diminish the therapeutic effect of Nivolumab. *Risk D: Consider therapy modification*

Ocrelizumab: May enhance the immunosuppressive effect of Immunosuppressants. *Risk C: Monitor therapy*

Ospemifene: CYP2C9 Inhibitors (Strong) may increase the serum concentration of Ospemifene. *Risk C: Monitor therapy*

Palifermin: May enhance the adverse/toxic effect of Antineoplastic Agents. Specifically, the duration and severity of oral mucositis may be increased. Management: Do not administer palifermin within 24 hours before, during infusion of, or within 24 hours after administration of myelotoxic chemotherapy. *Risk D: Consider therapy modification*

Parecoxib: CYP2C9 Inhibitors (Strong) may increase the serum concentration of Parecoxib. *Risk C: Monitor therapy*

Phenytoin: Capecitabine may increase the serum concentration of Phenytoin. *Risk D: Consider therapy modification*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Promazine: May enhance the myelosuppressive effect of Myelosuppressive Agents. *Risk C: Monitor therapy*

Proton Pump Inhibitors: May diminish the therapeutic effect of Capecitabine. *Risk C: Monitor therapy*

Ramelteon: CYP2C9 Inhibitors (Strong) may increase the serum concentration of Ramelteon. *Risk C: Monitor therapy*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider therapy modification*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor therapy*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Tetrahydrocannabinol: CYP2C9 Inhibitors (Strong) may increase the serum concentration of Tetrahydrocannabinol. *Risk C: Monitor therapy*

Tofacitinib: Immunosuppressants may enhance the immunosuppressive effect of Tofacitinib. Management: Concurrent use with antirheumatic doses of methotrexate or nonbiologic disease modifying antirheumatic drugs (DMARDs) is permitted, and this warning seems particularly focused on more potent immunosuppressants. *Risk X: Avoid combination*

Trastuzumab: May enhance the neutropenic effect of Immunosuppressants. *Risk C: Monitor therapy*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). Management: Vaccine efficacy may be reduced. Complete all age-appropriate vaccinations at least 2 weeks prior to starting an immunosuppressant. If vaccinated during immunosuppressant therapy, revaccinate at least 3 months after immunosuppressant discontinuation. *Risk D: Consider therapy modification*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. *Risk X: Avoid combination*

Vitamin K Antagonists (eg, warfarin): Capecitabine may increase the serum concentration of Vitamin K Antagonists. *Risk D: Consider therapy modification*

Food Interactions Food reduced the rate and extent of absorption of capecitabine. Management: Administer within 30 minutes after a meal.

Pregnancy Implications Based on animal reproduction studies and its mechanism of action, fetal harm may occur if capecitabine is administered during pregnancy. Pregnancy testing is recommended prior to therapy initiation. Women of reproductive potential should use effective contraception during treatment and for 6 months after the last dose. Males with female partners of reproductive potential should use effective contraception during treatment and for 3 months after the last dose.

Breast-Feeding Considerations It is not known if capecitabine is present in breast milk. Due to the potential for serious adverse reactions in the breastfed infant, breast-feeding is not recommended by the manufacturer during treatment and for 2 weeks after the last dose.

Monitoring Parameters Renal function should be estimated at baseline to determine initial dose. During therapy, CBC with differential, hepatic function, and renal function should be monitored. Monitor INR closely if receiving concomitant warfarin. Pregnancy test prior to treatment initiation (in females of reproductive potential). Monitor for diarrhea, dehydration, hand-foot syndrome, Stevens-Johnson syndrome, toxic epidermal necrolysis, stomatitis, and cardiotoxicity.

Mechanism of Action Capecitabine is a prodrug of fluorouracil. It undergoes hydrolysis in the liver and tissues to form fluorouracil which is the active moiety. Fluorouracil is a fluorinated pyrimidine antimetabolite that inhibits thymidylate synthetase, blocking the methylation of deoxyuridylic acid to thymidylic acid, interfering with DNA, and to a lesser degree, RNA synthesis. Fluorouracil appears to be phase specific for the G_1 and S phases of the cell cycle.

Pharmacodynamics/Kinetics

Absorption: Rapid and extensive (rate and extent reduced by food)

Protein binding: <60%; ~35% to albumin

Metabolism:

Hepatic: Inactive metabolites: 5′-deoxy-5-fluorocytidine, 5′-deoxy-5-fluorouridine

Tissue: Enzymatically metabolized to fluorouracil, which is then metabolized to active metabolites, 5-fluoroxyuridine monophosphate (F-UMP) and 5-5-fluoro-2'-deoxyuridine-5'-O-monophosphate (F-dUMP)

Half-life elimination: ~0.75 hour

Time to peak: 1.5 hours; Fluorouracil: 2 hours

Excretion: Urine (96%, 57% as α-fluoro-β-alanine; <3% as unchanged drug); feces (<3%)

Pricing: US

Tablets (Capecitabine Oral)

150 mg (60): $704.22

500 mg (120): $4694.24

Tablets (Xeloda Oral)

150 mg (60): $976.15

500 mg (120): $6506.77

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

Ai Bin (CN); Apecitab (AR); Arxeda (RO); Capebina (VN); Capecitabina (PE); Capetero (PH); Capibine (IN); Capit (LK); Captabine (BD, LK); Capvex (PH); Catacibin (PH); Caxeta (LK, PH); Cipatin (TR); Coloxet (HU); Ecansya (HU, MT); Intacape (TH); Kapetero (UA); Kapetsybeks (UA); Kaponko (UA); Kseloda (UA); Naprocap (PH); Xalvobin (HR, HU); Xelcip (ES); Xelobig (KR); Xelocan (KR); Xeloda (AE, AR, AT, AU, BB, BE, BF, BG, BH, BJ, BM, BR, BS, BZ, CH, CI, CL, CN, CO, CR, CU, CY, CZ, DE, DK, DO, EC, EE, ES, ET, FI, FR, GB, GH, GM, GN, GR, GT, GY, HK, HN, HR, HU, IE, IL, IS, IT, JM, JO, KE, KR, KW, LB, LK, LR, LT, LU, MA, ML, MR, MT, MU, MW, MX, MY, NE, NG, NI, NL, NO, NZ, PA, PH, PK, PL, PT, PY, QA, RO, RU, SA, SC, SD, SE, SG, SI, SK, SL, SN, SR, SV, TH, TN, TR, TT, TW, UG, UY, VE, VN, ZA, ZM, ZW); Xeltabine (PH, VN); Xitabin (BD, LK); Zapecine (ES)

REFERENCES

1. *Bachelot T, Romieu G, Campone M, et al, "Lapatinib Plus Capecitabine in Patients With Previously Untreated Brain*

Metastases From HER2-Positive Metastatic Breast Cancer (LANDSCAPE): A Single-Group Phase 2 Study," Lancet Oncol, 2013, 14(1):64-71. [PubMed 23122784]

2. *Bamat MK, Tremmel R, von Borstel R, et al. Clinical experience with uridine triacetate for 5-FU overexposure: an update [abstract e20592 from 2013 ASCO Annual Meeting]. J Clin Oncol. 2013;31(18s):e20592.*
3. *Bang YJ, Van Cutsem E, Feyereislova A, et al, "Trastuzumab in Combination With Chemotherapy Versus Chemotherapy Alone for Treatment of HER2-Positive Advanced Gastric or Gastro-Oesophageal Junction Cancer (ToGA): A Phase 3, Open-Label, Randomised Controlled Trial," Lancet, 2010, 376(9742):687-97. [PubMed 20728210]*
4. *Bartsch R, Wenzel C, Altorjai G, et al, "Capecitabine and Trastuzumab in Heavily Pretreated Metastatic Breast Cancer," J Clin Oncol, 2007, 25(25):3853-8. [PubMed 17679724]*
5. *Cartwright TH, Cohn A, Varkey JA, et al, "Phase II Study of Oral Capecitabine in Patients With Advanced or Metastatic Pancreatic Cancer," J Clin Oncol, 2002, 20(1):160-4. [PubMed 11773165]*
6. *Cassidy J, Clarke S, Díaz-Rubio E, et al, "Randomized Phase III Study of Capecitabine Plus Oxaliplatin Compared With Fluorouracil/Folinic Acid Plus Oxaliplatin as First-Line Therapy for Metastatic Colorectal Cancer," J Clin Oncol, 2008, 26(12):2006-12. [PubMed 18421053]*
7. *Cassidy J, Tabernero J, Twelves C, et al, "XELOX (Capecitabine Plus Oxaliplatin): Active First-Line Therapy for Patients With Metastatic Colorectal Cancer," J Clin Oncol, 2004, 22(11):2084-91. [PubMed 15169795]*
8. *Cassidy J, Twelves C, Van Cutsem E, et al. First-line oral capecitabine therapy in metastatic colorectal cancer: a favorable safety profile compared with intravenous 5-fluorouracil/leucovorin. Ann Oncol. 2002;13(4):566-575. [PubMed 12056707]*
9. *Cunningham D, Chau I, Stocken DD, et al, "Phase III Randomized Comparison of Gemcitabine versus Gemcitabine Plus Capecitabine in Patients With Advanced Pancreatic Cancer," J Clin Oncol, 2009, 27(33):5513-8. [PubMed 19858379]*
10. *Cunningham D, Starling N, Rao S, et al, "Capecitabine and Oxaliplatin for Advanced Esophagogastric Cancer," N Engl J Med, 2008, 358(1):36-46. [PubMed 18172173]*
11. *Dahan L, Ciccolini J, Evrard A, et al, "Sudden Death Related to Toxicity in a Patient on Capecitabine and Irinotecan Plus Bevacizumab Intake: Pharmacogenetic Implications," J Clin Oncol, 2012, 30(4):e41-4. [PubMed 22184401]*
12. *Ecklund JW, Trifilio S, and Mulcahy MF, "Chemotherapy Dosing in the Setting of Liver Dysfunction," Oncology (Williston Park), 2005, 19(8):1057-63. [PubMed 16131047]*
13. *Fine RL, Fogelman DR, Schreibman SM, et al, "The Gemcitabine, Docetaxel,and Capecitabine (GTX) Regimen for Metastatic Pancreatic Cancer: A Retrospective Analysis," Cancer Chemother Pharmacol, 2008, 61(1):167-75. [PubMed 17440727]*
14. *Geyer CE, Forster J, Lindquist D, et al, "Lapatinib Plus Capecitabine for HER2-Positive Advanced Breast Cancer," N Engl J Med, 2006, 355(26):2733-43. [PubMed 17192538]*
15. *Griggs JJ, Mangu PB, Anderson H, et al, "Appropriate Chemotherapy Dosing For Obese Adult Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline," J Clin Oncol, 2012, 30(13):1553-61. [PubMed 22473167]*
16. *Hainsworth JD, Spigel DR, Burris HA 3rd, et al, "Oxaliplatin and Capecitabine in the Treatment of Patients With Recurrent or Refractory Carcinoma of Unknown Primary Site: A Phase 2 Trial of the Sarah Cannon Oncology Research Consortium," Cancer, 2010, 116(10):2448-54. [PubMed 20209610]*
17. *Haller DG, Cassidy J, Clarke S, et al, "Potential Regional Differences for the Tolerability Profiles of Fluoropyrimidines," J Clin Oncol, 2008, 26(13):2118-23. [PubMed 18445840]*
18. *Haller DG, Tabernero J, Maroun J, et al, "Capecitabine Plus Oxaliplatin Compared With Fluorouracil and Folinic Acid as Adjuvant Therapy for Stage III Colon Cancer," J Clin Oncol, 2011, 29(11):1465-71. [PubMed 21383294]*
19. *Hennig IM, Naik JD, Brrown S, et al, "Severe Sequence-Specific Toxicity When Capecitabine Is Given After Fluorouracil and Leucovorin," J Clin Oncol, 2008, 26(20):3411-7. [PubMed 18612156]*
20. *Hezel AF and Zhu AX, "Systemic Therapy for Biliary Tract Cancers," Oncologist, 2008, 13(4):415-23. [PubMed 18448556]*
21. *Hoff PM, Ansari R, Batist G, et al, "Comparison of Oral Capecitabine Versus Intravenous Fluorouracil Plus Leucovorin as First-Line Treatment in 605 Patients With Metastatic Colorectal Cancer: Results of a Randomized Phase III Study," J Clin Oncol, 2001, 19(8):2282-92. [PubMed 11304782]*

22. *Hofheinz RD, Wenz F, Post S, et al, "Chemoradiotherapy With Capecitabine versus Fluorouracil for Locally Advanced Rectal Cancer: A Randomised, Multicentre, Non-Inferiority, Phase 3 Trial," Lancet Oncol, 2012, 13(6):579-88. [PubMed 22503032]*

23. *Hong YS, Song SY, Lee SI, et al, "A Phase II Trial of Capecitabine in Previously Untreated Patients With Advanced And/Or Metastatic Gastric Cancer," Ann Oncol, 2004, 15(9):1344-7. [PubMed 15319239]*

24. *Janus N, Thariat J, Boulanger H, et al, "Proposal for Dosage Adjustment and Timing of Chemotherapy in Hemodialyzed Patients," Ann Oncol, 2010, 21(7):1395-403. [PubMed 20118214]*

25. *Javle MM, Yang G, Nwogu CE, et al, "Capecitabine, Oxaliplatin, and Radiotherapy: A Phase 1B Neoadjuvant Study for Esophageal Cancer With Gene Expression Analysis," Cancer Invest, 2009, 27(2):193-200. [PubMed 19235592]*

26. *Judson IR, Beale PJ, Trigo JM, et al, "A Human Capecitabine Excretion Balance and Pharmacokinetic Study After Administration of a Single Oral Dose of ^{14}C-Labelled Drug," Invest New Drugs, 1999, 17(1):49-56. [PubMed 15173095]*

27. *Kang YK, Kang WK, Shin DB, et al, "Capecitabine/Cisplatin Versus 5-Fluorouracil/Cisplatin as First-Line Therapy in Patients With Advanced Gastric Cancer: A Randomised Phase III Noninferiority Trial," Ann Oncol, 2009, 20(4):666-73. [PubMed 19153121]*

28. *Kanie K, Plasencia AA, Dribben W, Tremmel R. Capecitabine [NACCT abstracts]. Clinical Toxicology. 2011;49:515-627.*

29. *Khorana AA, Mangu PB, Berlin J, et al. Potentially curable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline update [published online ahead of print April 11, 2107]. J Clin Oncol. 2017. doi: 10.1200/JCO.2017.72.4948. [PubMed 28398845]*

30. *Kim TW, Chang HM, Kang HJ, et al, "Phase II Study of Capecitabine Plus Cisplatin as First-Line Chemotherapy in Advanced Biliary Cancer," Ann Oncol, 2003, 14(7):1115-20. [PubMed 12853355]*

31. *Knox JJ, Hedley D, Oza A, et al, "Combining Gemcitabine and Capecitabine in Patients With Advanced Biliary Cancer: A Phase II Trial," J Clin Oncol, 2005, 23(10):2332-8. [PubMed 15800324]*

32. *Lee HS, Choi Y, Hur WJ, et al, "Pilot Study of Postoperative Adjuvant Chemoradiation for Advanced Gastric Cancer: Adjuvant 5-FU/Cisplatin and Chemoradiation With Capecitabine," World J Gastroenterol, 2006, 12(4):603-7. [PubMed 16489675]*

33. *Lee SS, Kim SB, Park SI, et al, "Capecitabine and Cisplatin Chemotherapy (XP) Alone or Sequentially Combined Chemoradiotherapy Containing XP Regimen in Patients With Three Different Settings of Stage IV Esophageal Cancer," Jpn J Clin Oncol, 2007, 37(11):829-35. [PubMed 17951334]*

34. *McGavin JK and Goa KL, "Capecitabine: A Review of Its Use in the Treatment of Advanced or Metastatic Colorectal Cancer," Drugs, 2001, 61(15):2309-26. [PubMed 11772141]*

35. *Meulendijks D, Dewit L, Tomasoa NB, et al. Chemoradiotherapy with capecitabine for locally advanced anal carcinoma: an alternative treatment option. Br J Cancer 2014;111(9):1726-1733. [PubMed 25167226]*

36. *Morgan C, Tillett T, Braybrooke J, et al, "Management of Uncommon Chemotherapy-Induced Emergencies," Lancet Oncol, 2011, 12(8):806-14. [PubMed 21276754]*

37. *Nehls O, Oettle H, Hartmann JT, et al, "Capecitabine Plus Oxaliplatin as First-Line Treatment in Patients With Advanced Biliary System Adenocarcinoma: A Prospective Multicentre Phase II Trial," Br J Cancer, 2008, 98(2):309-15. [PubMed 18182984]*

38. *Neoptolemos JP, Palmer DH, Ghaneh P, et al. Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4): a multicentre, open-label, randomised, phase 3 trial. Lancet. 2017;389(10073):1011-1024. [PubMed 28129987]*

39. *O'Shaughnessy J, Miles D, Vukelja S, et al, "Superior Survival With Capecitabine Plus Docetaxel Combination Therapy in Anthracycline-Pretreated Patients With Advanced Breast Cancer: Phase III Trial Results," J Clin Oncol, 2002, 20(12):2812-23. [PubMed 12065558]*

40. *Oliveira SC, Moniz CM, Riechelmann R, et al. Phase II study of capecitabine in substitution of 5-FU in the chemoradiotherapy regimen for patients with localized squamous cell carcinoma of the anal canal. J Gastrointest Cancer. 2016;47(1):75-81. [PubMed 26691173]*

41. *Page RL 2nd, O'Bryant CL, Cheng D, et al; American Heart Association Clinical Pharmacology and Heart Failure and Transplantation Committees of the Council on Clinical Cardiology; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular and Stroke Nursing; and Council on Quality of Care and Outcomes Research. Drugs That May Cause or Exacerbate Heart Failure: A Scientific Statement From the American Heart Association [published*

correction appears in Circulation. 2016;134(12):e261]. Circulation. 2016;134(6):e32-e69. doi: 10.1161/CIR.0000000000000426. [PubMed 27400984]

42. *Poole C, Gardiner J, Twelves C, et al. Effect of renal impairment on the pharmacokinetics and tolerability of capecitabine (Xeloda) in cancer patients. Cancer Chemother Pharmacol. 2002;49(3):225-234. [PubMed 11935215]*
43. *Schmoll HF, Cartwright T, Tabernero J, et al, "Phase III Trial of Capecitabine Plus Oxaliplatin as Adjuvant Therapy for Stage III Colon Cancer: A Planned Safety Analysis in 1,864 Patients," J Clin Oncol, 2007, 25(1):102-9. [PubMed 17194911]*
44. *Schneider BJ, El-Rayes B, Muler JH, et al. Phase II trial of carboplatin, gemcitabine, and capecitabine in patients with carcinoma of unknown primary site. Cancer. 2007;110(4):770-775. [PubMed 17594717]*
45. *Strosberg JR, Fine RL, Choi J, et al, "First-line Chemotherapy With Capecitabine and Temozolamide in Patients With Metastatic Pancreatic Endocrine Carcinomas," Cancer, 2011, 117(2):268-75. [PubMed 20824724]*
46. *Sumpter K, Harper-Wynne C, Cunningham D, et al, "Report of Two Protocol Planned Interim Analyses in a Randomized Multicenter Phase III Study Comparing Capecitabine With Fluorouracil and Oxaliplatin With Cisplatin in Patients With Advanced Oesophagogastric Cancer Receiving ECF," Br J Cancer, 2005, 92(11):1976-1983. [PubMed 15928658]*
47. *Superfin D, Iannucci AA, and Davies AM, "Commentary: Oncologic Drugs in Patients With Organ Dysfunction: A Summary," Oncologist, 2007;12(9):1070-1983. [PubMed 17914077]*
48. *Thind G, Johal B, Follwell M, et al. Chemoradiation with capecitabine and mitomycin-C for stage I-III anal squamous cell carcinoma. Radiat Oncol. 2014;9:124. [PubMed 24885554]*
49. *Thomas ES, Gomez HL, Li RK, et al, "Ixabepilone Plus Capecitabine for Metastatic Breast Cancer Progressing After Anthracycline and Taxane Treatment," J Clin Oncol, 2007, 25(33):5210-7. [PubMed 17968020]*
50. *Twelves C, Wong A, Nowacki MP, et al, "Capecitabine as Adjuvant Treatment for Stage III Colon Cancer," N Engl J Med, 2005, 352(26):2696-704. [PubMed 15987918]*
51. *US Department of Health and Human Services; Centers for Disease Control and Prevention; National Institute for Occupational Safety and Health. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2016. http://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf. Updated September 2016. Accessed October 5, 2016.*
52. *Van Cutsem E, Twelves C, Cassidy J, et al, "Oral Capecitabine Compared With Intravenous Fluorouracil Plus Leucovorin in Patients With Metastatic Colorectal Cancer: Results of a Large Phase III Study," J Clin Oncol, 2001, 19(21):4097-106. [PubMed 11689577]*
53. *Videnovic A, Semenov I Chua-Adajar R, et al, "Capecitabine-Induced Multifocal Leukoencephalopathy: A Report of Five Cases," Neurology, 2005, 65(11):1792-4. [PubMed 16237130]*
54. *von Borstel R, O'Neil J, Bamat M. Vistonuridine: An orally administered, life-saving antidote for 5-fluorouracil (5FU) overdose [abstract 9616]. J Clin Oncol. 2009;27(15s):9616.*
55. *Wolf JK, Bodurka DC, Verschraegen C, et al, "A Phase II Trial of Oral Capecitabine in Patients With Platinum- and Taxane-Refractory Ovarian, Fallopian Tube, or Peritoneal Cancer," Gynecol Oncol, 2006, 102(3):468-74. [PubMed 16516276]*
56. *Xeloda (capecitabine) [prescribing information]. South San Francisco, CA: Genentech USA, Inc; December 2016.*
57. *Xeloda (capecitabine) [product monograph]. Mississauga, Ontario: Hoffmann-La Roche Limited; August 2016.*
58. *Xiong HQ, Varadhachary GR, Blais JC, et al, "Phase 2 Trial of Oxaliplatin Plus Capecitabine (XELOX) as Second-Line Therapy for Patients With Advanced Pancreatic Cancer," Cancer, 2008, 113(8):2046-52. [PubMed 18756532]*
59. *Yang YK, Kang WK, Shin DB, et al, "Capecitabine/Cisplatin versus 5-Fluorouracil/Cisplatin as First-Line Therapy in Patients With Advanced Gastric Cancer: A Randomized Phase III Noninferiority Trial," Ann Oncol, 2009, 20(4):666-73. [PubMed 19153121]*

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