Gemcitabine: Drug information

(For additional information see "Gemcitabine: Patient drug information" and see "Gemcitabine: Pediatric drug information")

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

Brand Names: US

Gemzar

Brand Names: Canada

Gemcitabine For Injection; Gemcitabine For Injection Concentrate; Gemcitabine For Injection, USP; Gemcitabine Hydrochloride For Injection; Gemcitabine Injection; Gemcitabine Sun For Injection; Gemzar

Pharmacologic Category

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

Dosing: Adult

Note: Prolongation of the infusion duration >60 minutes and administration more frequently than once weekly have been shown to increase toxicity.

Breast cancer, metastatic: IV: 1250 mg/m^2 over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with paclitaxel) **or** (off-label dosing; as a single agent) 800 mg/m^2 over 30 minutes days 1, 8, and 15 of a 28-day treatment cycle (Carmichael 1995)

Non-small cell lung cancer, locally advanced or metastatic: IV: 1000 mg/m^2 over 30 minutes days 1, 8, and 15; repeat cycle every 28 days (in combination with cisplatin) **or** 1250 mg/m^2 over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with cisplatin) **or** (off-label dosing/combination) 1000 mg/m^2 over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with carboplatin) for up to 4 cycles (Grønberg 2009) **or** (off-label combination) 1000 mg/m^2 over 30 minutes days 1, 8, and 15; repeat cycle every 28 days (in combination with carboplatin) for up to 4 cycles (Danson 2003) **or** (off-label combination) 1000 mg/m^2 over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with docetaxel) for 8 cycles (Pujol 2005) **or** (off-label combination) 1000 mg/m^2 days 1, 8, and 15; repeat cycle every 28 days (in combination with vinorelbine) for 6 cycles (Greco 2007)

Ovarian cancer, advanced: IV: 1000 mg/m^2 over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with carboplatin) **or** (off-label dosing; as a single agent) 1000 mg/m^2 over 30 to 60 minutes days 1 and 8; repeat cycle every 21 days (Mutch 2007)

Pancreatic cancer (locally advanced or metastatic): IV: Initial: 1000 mg/m^2 over 30 minutes once weekly for 7 weeks followed by 1 week rest; then once weekly for 3 weeks out of every 4 weeks **or** (off-label combinations) 1000 mg/m^2 over 30 minutes weekly for up to 7 weeks followed by 1 week rest; then weekly for 3 weeks out of every 4 weeks (in combination with erlotinib) (Moore 2007) **or** 1000 mg/m^2 over 30 minutes days 1, 8, and 15 every 28 days (in combination with capecitabine) (Cunningham 2009) **or** 1000 mg/m^2 over 30 minutes days 1 and 15 every 28 days (in combination with cisplatin) (Heinemann 2006) **or** 1000 mg/m^2 infused at 10 mg/m^2/minute every 14 days (in combination with oxaliplatin) (Louvet

2005) **or** 1000 mg/m^2 days 1, 8, and 15 every 28 days (in combination with paclitaxel [protein bound]) (Von Hoff 2013)

Pancreatic cancer (adjuvant therapy) (off-label use): IV: 1000 mg/m^2 on days 1, 8 and 15 every 28 days (in combination with capecitabine) 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]).

Bladder cancer (off-label use):

Advanced or metastatic: IV: 1000 mg/m^2 over 30 to 60 minutes days 1, 8, and 15; repeat cycle every 28 days (in combination with cisplatin) (von der Maase 2000) **or** 1000 mg/m^2 over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with carboplatin) until disease progression or unacceptable toxicity (De Santis 2012)

Transitional cell carcinoma: Intravesicular instillation: 2000 mg (in 100 mL NS; retain for 1 hour) twice weekly for 3 weeks; repeat cycle every 4 weeks for at least 2 cycles (Dalbagni 2006)

Cervical cancer, recurrent or persistent (off-label use): IV: 1000 mg/m^2 days 1 and 8; repeat cycle every 21 days (in combination with cisplatin) (Monk 2009) **or** 1250 mg/m^2 over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with cisplatin) (Burnett 2000) **or** 800 mg/m^2 over 30 minutes days 1, 8, and 15; repeat cycle every 28 days (as a single-agent) (Schilder 2005) **or** 800 mg/m^2 days 1 and 8; repeat cycle every 28 days (in combination with cisplatin) (Brewer 2006)

Head and neck cancer, nasopharyngeal (off-label use): IV: 1000 mg/m^2 over 30 minutes days 1, 8, and 15 every 28 days (Zhang 2008) **or** 1000 mg/m^2 over 30 minutes days 1 and 8 every 21 days (in combination with vinorelbine) (Chen 2012)

Hepatobiliary cancer, advanced (off-label use): IV: 1000 mg/m^2 over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with cisplatin) (Valle 2010) **or** 1000 mg/m^2 over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with capecitabine) (Knox 2005) **or** 1000 mg/m^2 infused at 10 mg/m^2/minute every 2 weeks (in combination with oxaliplatin) (Andre 2004)

Hodgkin lymphoma, relapsed (off-label use): IV: 1000 mg/m^2 (800 mg/m^2 for post-transplant patients) over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with vinorelbine and doxorubicin liposomal) (Bartlett 2007) **or** 800 mg/m^2 days 1 and 4; repeat cycle every 21 days (in combination with ifosfamide, mesna, vinorelbine, and prednisolone) (Santoro 2007)

Malignant pleural mesothelioma (off-label use; in combination with cisplatin): IV: 1000 mg/m^2 over 30 minutes days 1, 8 and 15 every 28 days for up to 6 cycles (Nowak 2002) **or** 1250 mg/m^2 over 30 minutes days 1 and 8 every 21 days for up to 6 cycles (van Haarst 2002)

Non-Hodgkin lymphoma, refractory (off-label use): IV: 1000 mg/m^2 over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with cisplatin and dexamethasone) (Crump 2004) **or** 1000 mg/m^2 every 15 to 21 days (in combination with oxaliplatin and rituximab) (Lopez 2008)

Sarcoma (off-label uses): IV:

Ewing's sarcoma, refractory: 675 mg/m^2 over 90 minutes days 1 and 8; repeat cycle every 21 days (in combination with docetaxel) (Navid 2008)

Osteosarcoma, refractory: 675 mg/m^2 over 90 minutes days 1 and 8; repeat cycle every 21 days (in combination with docetaxel) (Navid 2008) **or** 1000 mg/m^2 weekly for 7 weeks followed by 1 week

rest; then weekly for 3 weeks out of every 4 weeks (Merimsky 2000)

Soft tissue sarcoma, advanced: 800 mg/m^2 over 90 minutes days 1 and 8; repeat cycle every 21 days (in combination with vinorelbine) (Dileo 2007) **or** 675 mg/m^2 over 90 minutes days 1 and 8; repeat cycle every 21 days (in combination with docetaxel) (Leu 2004) **or** 900 mg/m^2 over 90 minutes days 1 and 8; repeat cycle every 21 days (in combination with docetaxel) (Maki 2007)

Small cell lung cancer, refractory or relapsed (off-label use): IV: 1000 to 1250 mg/m^2 over 30 minutes days 1, 8, and 15 every 28 days (as a single agent) (Masters 2003)

Testicular cancer, refractory germ cell (off-label use): IV: 1000 to 1250 mg/m^2 over 30 minutes days 1 and 8 every 21 days (in combination with oxaliplatin) (DeGiorgi 2006; Kohllmannsberger 2004; Pectasides 2004) **or** 1000 mg/m^2 over 30 minutes days 1, 8, and 15 every 28 days for up to 6 cycles (in combination with paclitaxel) (Hinton 2002) **or** 800 mg/m^2 over 30 minutes days 1 and 8 every 21 days (in combination with oxaliplatin and paclitaxel) (Bokemeyer 2008)

Unknown-primary, adenocarcinoma (off-label use): IV: 1250 mg/m^2 days 1 and 8 every 21 days (in combination with cisplatin) (Culine 2003) **or** 1000 mg/m^2 over 30 minutes days 1 and 8 every 21 days for up to 6 cycles (in combination with docetaxel) (Pouessel 2004)

Uterine cancer (off-label use): IV: 900 mg/m^2 over 90 minutes days 1 and 8 every 21 days (in combination with docetaxel) (Hensley 2008) **or** 1000 mg/m^2 over 30 minutes days 1, 8, and 15 every 28 days (Look 2004)

Dosing: Pediatric

(For additional information see "Gemcitabine: Pediatric drug information")

Note: Prolongation of the infusion duration >60 minutes and administration more frequently than once weekly have been shown to increase toxicity. Refer to specific references for ages of populations studied:

Germ cell tumor, refractory (off-label use): IV: 1000 mg/m^2 over 30 minutes days 1, 8, and 15 every 28 days (in combination with paclitaxel) for up to 6 cycles (Hinton 2002)

Hodgkin lymphoma, relapsed (off-label use): IV: 1000 mg/m^2 over 100 minutes days 1 and 8; repeat cycle every 21 days (in combination with vinorelbine) (Cole 2009) **or** 800 mg/m^2 days 1 and 4; repeat cycle every 21 days (in combination with ifosfamide, mesna, vinorelbine, and prednisolone) (Santoro 2007)

Sarcomas (off-label use): IV:

Ewing's sarcoma, refractory: 675 mg/m^2 over 90 minutes days 1 and 8; repeat cycle every 21 days (in combination with docetaxel) (Navid 2008)

Osteosarcoma, refractory: 675 mg/m^2 over 90 minutes days 1 and 8; repeat cycle every 21 days (in combination with docetaxel) (Navid 2008) **or** 1000 mg/m^2 weekly for 7 weeks followed by 1 week rest; then weekly for 3 weeks out of every 4 weeks (Merimsky 2000)

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

There are no dosage adjustments provided in the manufacturer's labeling; use with caution in patients with pre-existing renal dysfunction. Discontinue if severe renal toxicity or

hemolytic uremic syndrome (HUS) occur during gemcitabine treatment.

Mild-to-severe renal impairment: No dosage adjustment necessary (Janus 2010; Li 2007).

ESRD (on hemodialysis): Hemodialysis should begin 6 to 12 hours after gemcitabine infusion (Janus 2010; Li 2007).

Dosing: Hepatic Impairment

There are no dosage adjustments provided in the manufacturer's labeling; use with caution. Discontinue if severe hepatotoxicity occurs during gemcitabine treatment. The following adjustments have been reported:

Transaminases elevated (with normal bilirubin): No dosage adjustment necessary (Venook 2000).

Serum bilirubin >1.6 mg/dL: Use initial dose of 800 mg/m^2; may escalate if tolerated (Ecklund 2005; Floyd 2006; Venook 2000).

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).

Dosing: Adjustment for Toxicity

Nonhematologic toxicity (all indications):

Hold or decrease gemcitabine dose by 50% for the following: Severe (grade 3 or 4) nonhematologic toxicity until resolved (excludes nausea, vomiting, or alopecia [no dose modifications recommended])

Permanently discontinue gemcitabine for any of the following: Unexplained dyspnea (or other evidence of severe pulmonary toxicity), severe hepatotoxicity, hemolytic uremic syndrome (HUS), capillary leak syndrome (CLS), posterior reversible encephalopathy syndrome (PRES)

Hematologic toxicity:

Breast cancer:

Day 1:

Absolute granulocyte count (AGC) ≥1500/mm^3 and platelet count ≥100,000/mm^3: Administer 100% of full dose

AGC <1500/mm^3 or platelet count <100,000/mm^3: Hold dose

Day 8:

AGC ≥1200/mm^3 and platelet count >75,000/mm^3: Administer 100% of full dose

AGC 1000 to 1199/mm^3 or platelet count 50,000 to 75,000/mm^3: Administer 75% of full dose

AGC 700 to 999/mm^3 and platelet count ≥50,000/mm^3: Administer 50% of full dose

AGC <700/mm^3 or platelet count <50,000/mm^3: Hold dose

Non-small cell lung cancer (cisplatin dosage may also require adjustment):

AGC ≥1000/mm^3 and platelet count ≥100,000/mm^3: Administer 100% of full dose

AGC 500 to 999/mm^3 or platelet count 50,000 to 99,999/mm^3: Administer 75% of full dose

AGC <500/mm^3 or platelet count <50,000/mm^3: Hold dose

Ovarian cancer:

Day 1:

AGC ≥1500/mm^3 and platelet count ≥100,000/mm^3: Administer 100% of full dose

AGC <1500/mm^3 or platelet count <100,000/mm^3: Delay treatment cycle

Day 8:

AGC ≥1500/mm^3 and platelet count ≥100,000/mm^3: Administer 100% of full dose

AGC 1000 to 1499/mm^3 or platelet count 75,000 to 99,999/mm^3: Administer 50% of full dose

AGC <1000/mm^3 or platelet count <75,000/mm^3: Hold dose

Hematologic toxicity in previous cycle (dosing adjustment for subsequent cycles):

Initial occurrence: AGC <500/mm^3 for >5 days, AGC <100/mm^3 for >3 days, neutropenic fever, platelet count <25,000/mm^3, or cycle delay >1 week due to toxicity: Permanently reduce gemcitabine to 800 mg/m^2 on days 1 and 8.

Subsequent occurrence: AGC <500/mm^3 for >5 days, AGC <100/mm^3 for >3 days, neutropenic fever, platelet count <25,000/mm^3, or cycle delay >1 week due to toxicity: Permanently reduce gemcitabine to 800 mg/m^2 and administer on day 1 only.

Pancreatic cancer (locally advanced or metastatic):

AGC ≥1000/mm^3 and platelet count ≥100,000/mm^3: Administer 100% of full dose

AGC 500 to 999/mm^3 or platelet count 50,000 to 99,999/mm^3: Administer 75% of full dose

AGC <500/mm^3 or platelet count <50,000/mm^3: Hold dose

Dosage Forms

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

Solution, Intravenous:

Generic: 200 mg/5.26 mL (5.26 mL); 1 g/26.3 mL (26.3 mL); 2 g/52.6 mL (52.6 mL)

Solution, Intravenous [preservative free]:

Generic: 200 mg/5.26 mL (5.26 mL); 1 g/26.3 mL (26.3 mL); 2 g/52.6 mL (52.6 mL)

Solution Reconstituted, Intravenous:

Gemzar: 200 mg (1 ea); 1 g (1 ea)

Generic: 200 mg (1 ea); 1 g (1 ea); 2 g (1 ea)

Solution Reconstituted, Intravenous [preservative free]:

Generic: 200 mg (1 ea); 1 g (1 ea); 2 g (1 ea)

Generic Equivalent Available (US) Yes

Dosage Forms: Canada Information with regard to form, strength, and availability of products uniquely available in Canada but currently not available in the US. Refer also to Dosage forms.

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

Solution, Intravenous: 200 mg/5mL, 1 g/25 mL, 2 g/50 mL [40 mg/mL]

Solution, Intravenous: 200 mg/5.3 mL, 1 g/26.3 mL, 2 g/52.6 mL [38 mg/mL]

Solution Reconstituted, Intravenous: 200 mg, 1 g, 2 g

Administration Infuse over 30 minutes; for off-label uses, infusion times may vary (refer to specific references). **Note:** Prolongation of the infusion time >60 minutes has been shown to increase toxicity. Gemcitabine has been administered at a fixed-dose rate (FDR) infusion rate of 10 mg/m^2/minute to optimize the pharmacokinetics (off-label); prolonged infusion times increase the intracellular accumulation of the active metabolite, gemcitabine triphosphate (Ko 2006; Tempero 2003). Patients who receive gemcitabine FDR experience more grade 3/4 hematologic toxicity (Ko 2006; Poplin 2009).

For intravesicular (bladder) instillation (off-label route), gemcitabine was diluted in 50 to 100 mL normal saline; patients were instructed to retain in the bladder for 1 hour (Addeo 2010; Dalbaghi 2006)

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 double gloving, a protective gown, ventilated engineering controls (a class II biological safety cabinet or a compounding aseptic containment isolator), and closed system transfer devices (CSTDs) for preparation. Double gloving, a gown, and (if dosage form allows) CSTDs are required during administration (NIOSH 2016).

Use

Breast cancer: First-line treatment of metastatic breast cancer (in combination with paclitaxel) after failure of adjuvant chemotherapy which contained an anthracycline (unless contraindicated)

Non-small cell lung cancer (NSCLC): First-line treatment of inoperable, locally-advanced (stage IIIA or IIIB) or metastatic (stage IV) NSCLC (in combination with cisplatin)

Ovarian cancer: Treatment of advanced ovarian cancer (in combination with carboplatin) that has relapsed at least 6 months following completion of platinum-based chemotherapy

Pancreatic cancer (locally advanced or metastatic): First-line treatment of locally-advanced (nonresectable stage II or III) or metastatic (stage IV) pancreatic adenocarcinoma

Use: Off-Label

Pancreatic cancer (adjuvant therapy); Additional off-label uses

Medication Safety Issues

Sound-alike/look-alike issues:

Gemcitabine may be confused with gemtuzumab

Gemzar may be confused with Zinecard

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.

International issues:

In Canada, gemcitabine is available as a concentrated solution for injection in different strengths (38 mg/mL and 40 mg/mL), and a powder for reconstitution (final concentration of 38 mg/mL after reconstitution). Verify product concentration prior to preparation for administration.

Adverse Reactions

Frequency of adverse reactions reported for single-agent use of gemcitabine only; bone marrow depression is the dose-limiting toxicity.

>10%:

Cardiovascular: Peripheral edema (20%), edema (13%)

Central nervous system: Drowsiness (11%)

Dermatologic: Skin rash (30%), alopecia (15%)

Gastrointestinal: Nausea and vomiting (69%), diarrhea (19%), stomatitis (11%)

Genitourinary: Proteinuria (45%), hematuria (35%)

Hematologic & oncologic: Anemia (68%; grade 3: 7%; grade 4: 1%), neutropenia (63%; grade 3: 19%; grade 4: 6%), thrombocytopenia (24%; grade 3: 4%; grade 4: 1%), hemorrhage (17%; grade 3: <1%; grade 4: <1%)

Hepatic: Increased serum ALT (68%; grade 3: 8%, grade 4: 2%), increased serum AST (67%; grade 3: 6%; grade 4: 2%), increased serum alkaline phosphatase (55%; grade 3: 7%; grade 4: 2%), increased serum bilirubin (13%; grade 3: 2%, grade 4: <1%)

Infection: Infection (16%)

Renal: Increased blood urea nitrogen (16%)

Respiratory: Dyspnea (23%; grade 3: 3%; grade 4: <1%), flu-like symptoms (19%)

Miscellaneous: Fever (41%)

1% to 10%:

Central nervous system: Paresthesia (10%; grade 3: <1%)

Local: Injection site reaction (4%)

Renal: Increased serum creatinine (8%)

Respiratory: Bronchospasm (<2%)

<1%, postmarketing, and/or case reports (reported with single-agent use or with combination therapy): Adult respiratory distress syndrome, anaphylactoid reaction, anorexia, arthralgia, bullous skin disease, capillary leak syndrome, cardiac arrhythmia, cardiac failure, cellulitis, cerebrovascular accident (Kuenen 2002), constipation, desquamation, digital vasculitis, gangrene of skin or other tissue, hemolytic-uremic syndrome, hepatic failure, hepatic veno-occlusive disease, hepatotoxicity (rare), hyperglycemia, hypertension, hypocalcemia, hypotension, increased gamma-glutamyl transferase, interstitial pneumonitis, myocardial infarction, neuropathy, petechiae (Nishijima 2013; Zupancic 2007), pruritus (Curtis 2014), pulmonary edema, pulmonary fibrosis, radiation recall phenomenon, renal failure, respiratory failure, reversible posterior leukoencephalopathy syndrome, sepsis, supraventricular cardiac arrhythmia, thrombotic thrombocytopenic purpura (Nishijima 2013; Zupancic 2007)

Contraindications

Hypersensitivity to gemcitabine or any component of the formulation

Warnings/Precautions

Concerns related to adverse effects:

• Bone marrow suppression: May cause bone marrow suppression (neutropenia, thrombocytopenia, and anemia); myelosuppression is generally the dose-limiting toxicity and is increased when used in combination with other chemotherapy. Monitor blood counts; dosage adjustments are frequently required.

• Capillary leak syndrome: Capillary leak syndrome (CLS) with serious consequences has been reported, both with single-agent gemcitabine and with combination chemotherapy; discontinue if CLS develops.

• Hemolytic uremic syndrome: Hemolytic uremic syndrome (HUS) has been reported; may lead to renal failure and dialysis (including fatalities); monitor for evidence of anemia with microangiopathic hemolysis (elevation of bilirubin or LDH, reticulocytosis, severe thrombocytopenia, and/or renal failure) and monitor renal function at baseline and periodically during treatment. Permanently discontinue if HUS or severe renal impairment occurs; renal failure may not be reversible despite

discontinuation.

• Hepatotoxicity: Serious hepatotoxicity (including liver failure and death) has been reported (when used alone or in combination with other hepatotoxic medications); use in patients with hepatic impairment (history of cirrhosis, hepatitis, or alcoholism) or in patients with hepatic metastases may lead to exacerbation of hepatic impairment. Monitor hepatic function at baseline and periodically during treatment; consider dose adjustments with elevated bilirubin; discontinue if severe liver injury develops.

• Posterior reversible encephalopathy syndrome: Posterior reversible encephalopathy syndrome (PRES) has been reported, both with single-agent therapy and with combination chemotherapy. PRES may manifest with blindness, confusion, headache, hypertension, lethargy, seizure, and other visual and neurologic disturbances. If PRES diagnosis is confirmed (by MRI), discontinue therapy.

• Pulmonary toxicity: Pulmonary toxicity, including adult respiratory distress syndrome, interstitial pneumonitis, pulmonary edema, and pulmonary fibrosis, has been observed; may lead to respiratory failure (some fatal) despite discontinuation. Onset for symptoms of pulmonary toxicity may be delayed up to 2 weeks beyond the last dose. Discontinue for unexplained dyspnea (with or without bronchospasm) or other evidence of pulmonary toxicity.

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:

• Radiation therapy recipients: Not indicated for use with concurrent radiation therapy; radiation toxicity, including tissue injury, severe mucositis, esophagitis, or pneumonitis, has been reported with concurrent and nonconcurrent administration; has radiosensitizing activity when gemcitabine and radiation therapy are given together or ≤7 days apart; radiation recall may occur when gemcitabine and radiation therapy are given >7 days apart.

Other warnings/precautions:

• Infusion duration/frequency: Prolongation of the infusion duration >60 minutes or more frequent than weekly dosing have been shown to alter the half-life and increase toxicity (hypotension, flu-like symptoms, myelosuppression, weakness). A fixed-dose rate (FDR) infusion rate of 10 mg/m^2/minute has been studied in adults in order to optimize the pharmacokinetics (off-label); prolonged infusion times increase the intracellular accumulation of the active metabolite, gemcitabine triphosphate (Ko 2006; Tempero 2003). Patients who receive gemcitabine FDR experience more grade 3/4 hematologic toxicity (Ko 2006; Poplin 2009).

Metabolism/Transport Effects

None known.

Drug Interactions

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

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*

Bleomycin: Gemcitabine may enhance the adverse/toxic effect of Bleomycin. The risk of pulmonary toxicity may be increased. *Risk D: Consider therapy modification*

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*

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*

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

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*

Fluorouracil (Systemic): Gemcitabine may increase the serum concentration of Fluorouracil (Systemic). *Risk C: Monitor therapy*

Fluorouracil (Topical): Gemcitabine may increase the serum concentration of Fluorouracil (Topical). *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*

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*

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*

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*

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*

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*

Warfarin: Gemcitabine may enhance the anticoagulant effect of Warfarin. *Risk C: Monitor therapy*

Pregnancy Risk Factor

D (show table)

Pregnancy Implications

Adverse events were observed in animal reproduction studies. May cause fetal harm if administered during pregnancy; adverse effects in reproduction are anticipated based on the mechanism of action.

Breast-Feeding Considerations

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

Monitoring Parameters

CBC with differential and platelet count (prior to each dose); hepatic and renal function (prior to initiation of therapy and periodically, thereafter); monitor electrolytes, including potassium, magnesium, and calcium (when in combination therapy with cisplatin); monitor pulmonary function; signs/symptoms of capillary leak syndrome and posterior reversible encephalopathy syndrome

Mechanism of Action A pyrimidine antimetabolite that inhibits DNA synthesis by inhibition of DNA polymerase and ribonucleotide reductase, cell cycle-specific for the S-phase of the cycle (also blocks cellular progression at G1/S-phase). Gemcitabine is phosphorylated intracellularly by deoxycytidine kinase to gemcitabine monophosphate, which is further phosphorylated to active metabolites gemcitabine diphosphate and gemcitabine triphosphate. Gemcitabine diphosphate inhibits DNA synthesis by inhibiting ribonucleotide reductase; gemcitabine triphosphate incorporates into DNA and inhibits DNA polymerase.

Pharmacodynamics/Kinetics

Distribution: Widely distributed into tissues; present in ascitic fluid; V_d: Infusions <70 minutes: 50 L/m^2; Long infusion times (70 to 285 minutes): 370 L/m^2

Protein binding: Negligible

Metabolism: Metabolized intracellularly by nucleoside kinases to the active diphosphate (dFdCDP) and triphosphate (dFdCTP) nucleoside metabolites

Half-life elimination:

Gemcitabine: Infusion time ≤70 minutes: 42 to 94 minutes; infusion time 3 to 4 hours: 4 to 10.5 hours (affected by age and gender)

Metabolite (gemcitabine triphosphate), terminal phase: 1.7 to 19.4 hours

Time to peak, plasma: 30 minutes after completion of infusion

Excretion: Urine (92% to 98%; primarily as inactive uracil metabolite); feces (<1%)

Pricing: US

Solution (Gemcitabine HCl Intravenous)

1 g/26.3 mL (26.3 mL): $53.56

2 g/52.6 mL (52.6 mL): $107.40

200 mg/5.26 mL (5.26 mL): $10.72

Solution (reconstituted) (Gemcitabine HCl Intravenous)

1 g (1): $90.00

2 g (1): $123.18

200 mg (1): $12.00

Solution (reconstituted) (Gemzar Intravenous)

1 g (1): $889.14

200 mg (1): $177.83

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 Abine (AR); Bigemax (VN); Cytogem (ID); DBL (TW); Gembine (KR); Gembio (PH); Gemcetin (BD); Gemcibine (KR); Gemcikal (ID, PH); Gemcimax (TH); Gemcit (BR, KR, LK, PE, PH, TH); Gemcite (IN); Gemezar (JO); Gemflor (TW); Gemhope (PH); Gemita (LK, PH, SG, TH, TW); Gemmis (TW); Gemoxen (BD); Gemresec (SG); Gemtan (KR); Gemtavis (ID); Gemtero (SG, TH, ZW); Gemtin (TH); Gemtra (KR); Gemtro (AR); Gemxit (MX); Gemzar (AE, AT, AU, BE, BF, BG, BH, BJ, BO, BR, CH, CI, CL, CN, CO, CY, CZ, DE, DK, DO, EE, EG, ET, FI, FR, GB, GH, GM, GN, GR, HK, HR, HU, ID, IE, IL, IS, IT, KE, KR, KW, LB, LK, LR, LT, LU, MA, ML, MR, MT, MU, MW, MX, MY, NE, NG, NL, NO, NZ, PA, PE, PH, PK, PL, PR, PT, PY, QA, RO, RU, SA, SC, SD, SE, SG, SI, SK, SL, SN, TH, TN, TR, TW, TZ, UG, UY, VE, VN, ZA, ZM, ZW); Gercizar (LB); Getanosan (ID); Gezt (LB, PY); Gitrabin (HK, HR, PH, RO, SG); Hemtero (UA); Hemzar (UA); Meditabine (IL); Oncogem (LB); Oncoril (LK); Pamigen (CR, DO, EC, GT, HN, NI, PA, SV); Tsytohem (UA); Zarbin (MX); Zefei (PH)

REFERENCES

1. *Addeo R, Caraglia M, Bellini S, et al, "Randomized Phase III Trial on Gemcitabine versus Mytomicin in Recurrent Superficial Bladder Cancer: Evaluation of Efficacy and Tolerance," J Clin Oncol, 2010, 28(4):543-8. [PubMed 19841330]*
2. *Albain KS, Nag SM, Calderillo-Ruiz G, et al, "Gemcitabine Plus Paclitaxel versus Paclitaxel Monotherapy in Patients With Metastatic Breast Cancer and Prior Anthracycline Treatment," J Clin Oncol, 2008, 26(24):3950-7. [PubMed 18711184]*
3. *Andre T, Tournigand C, Rosmorduc O, et al, "Gemcitabine Combined With Oxaliplatin (GEMOX) in Advanced Biliary Tract Adenocarcinoma: A GERCOR Study," Ann Oncol, 2004, 15(9):1339-43. [PubMed 15319238]*
4. *Bao PQ, Ramanathan RK, Krasinkas A, et al. Phase II study of gemcitabine and erlotinib as adjuvant therapy for patients with resected pancreatic cancer. Ann Surg Oncol. 2011;18(4):1122-1129. [PubMed 21104328]*
5. *Bartlett NL, Niedzwiecki D, Johnson JL, et al, "Gemcitabine, Vinorelbine, and Pegylated Liposomal Doxorubicin (GVD), a Salvage Regimen in Relapsed Hodgkin's Lymphoma: CALGB 59804," Ann Oncol, 2007, 18(6):1071-9. [PubMed 17426059]*
6. *Bokemeyer C, Oechsle K, Honecker F, et al, "Combination Chemotherapy With Gemcitabine, Oxaliplatin, and Paclitaxel in Patients With Cisplatin-Refractory or Multiply Relapsed Germ-Cell Tumors: A Study of the German Testicular Cancer Study Group," Ann Oncol, 2008, 19(3):448-53. [PubMed 18006893]*
7. *Bredenfeld H, Franklin J, Nogova L, et al, "Severe Pulmonary Toxicity in Patients With Advanced-Stage Hodgkin's Disease Treated With a Modified Bleomycin, Doxorubicin, Cyclophosphamide, Vincristine, Procarbazine, Prednisone, and Gemcitabine (BEACOPP) Regimen is Probably Related to the Combination of Gemcitabine and Bleomycin: A Report of the German Hodgkin's Lymphoma Study Group," J Clin Oncol, 2004, 22(12):2424-9. [PubMed 15136597]*
8. *Brewer CA, Blessing JA, Nagourney RA, et al. Cisplatin plus gemcitabine in previously treated squamous cell carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. Gynecol Oncol. 2006;100(2):385-388. [PubMed 16271750]*
9. *Burnett AF, Roman LD, Garcia AA, "A Phase II Study of Gemcitabine and Cisplatin in Patients With Advanced, Persistent, or Recurrent Squamous Cell Carcinoma of the Cervix," Gynecol Oncol, 2000, 76(1):63-6. [PubMed 10620443]*
10. *Carmichael J, Possinger K, Phillip P, et al, "Advanced Breast Cancer: A Phase II Trial With Gemcitabine," J Clin Oncol, 1995, 13(11):2731-6. [PubMed 7595731]*
11. *Chen C, Wang FH, Wang ZQ, et al, "Salvage Gemcitabine-Vinorelbine Chemotherapy in Patients With Metastatic Nasopharyngeal Carcinoma Pretreated With Platinum-Based Chemotherapy," Oral Oncol, 2012, 48(11):1146-51. [PubMed 22748450]*
12. *Cole PD, Schwartz CL, Drachtman RA, et al, "Phase II Study of Weekly Gemcitabine and Vinorelbine for Children With*

Recurrent or Refractory Hodgkin's Disease: A Children's Oncology Group Report," J Clin Oncol, 2009, 27(9):1456-61. [PubMed 19224841]

13. *Correale P, Cerretani D, Marsili S, et al, "Gemcitabine Increases Systemic 5-Fluorouracil Exposure in Advanced Cancer Patients," Eur J Cancer, 2003, 39(11):1547-51. [PubMed 12855261]*
14. *Crump M, Baetz T, Couban S, et al, "Gemcitabine, Dexamethasone, and Cisplatin in Patients With Recurrent or Refractory Aggressive Histology B-Cell Non-Hodgkin Lymphoma: A Phase II Study by the National Cancer Institute of Canada Clinical Trials Group (NCIC-CTG)," Cancer, 2004, 101(8):1835-42. [PubMed 15386331]*
15. *Culine S, Lortholary A, Voigt JJ, et al, "Cisplatin in Combination With Either Gemcitabine or Irinotecan in Carcinomas of Unknown Primary Site: Results of a Randomized Phase II Study - Trial for the French Study Group on Carcinomas of Unknown Primary (GEFCAPI 01)," J Clin Oncol, 2003, 21(18):3479-82. [PubMed 12972523]*
16. *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]*
17. *Curtis S, Hong S, Gucalp R, Calvo M. Gemcitabine-induced pseudocellulitis in a patient with recurrent lymphedema: a case report and review of the current literature [published online January 21, 2014]. Am J Ther. [PubMed 24451298]*
18. *Dalbagni G, Russo P, Bochner B, et al, "Phase II Trial of Intravesical Gemcitabine in Bacille Calmette-Guerin-Refractory Transitional Cell Carcinoma of the Bladder," J Clin Oncol, 2006, 24(18):2729-34. [PubMed 16782913]*
19. *Danson S, Middleton MR, O'Byrne KJ, et al. Phase III trial of gemcitabine and carboplatin versus mitomycin, ifosfamide, and cisplatin or mitomycin, vinblastine, and cisplatin in patients with advanced nonsmall cell lung carcinoma. Cancer. 2003;98(3):542-553. [PubMed 12879472]*
20. *De Giorgi U, Rosti G, Aieta M, et al, "Phase II Study of Oxaliplatin and Gemcitabine Salvage Chemotherapy in Patients With Cisplatin-Refractory Nonseminomatous Germ Cell Tumor," Eur Urol, 2006, 50(5):1032-8. [PubMed 16757095]*
21. *De Santis M, Bellmunt J, Mead G, et al. Randomized phase II/III trial assessing gemcitabine/carboplatin and methotrexate/carboplatin/vinblastine in patients with advanced urothelial cancer who are unfit for cisplatin-based chemotherapy: EORTC study 30986. J Clin Oncol. 2012;30(2):191-199.*
22. *Dileo P, Morgan JA, Zahrieh D, et al, "Gemcitabine and Vinorelbine Combination Chemotherapy for Patients With Advanced Soft Tissue Sarcomas: Results of a Phase II Trial," Cancer, 2007, 109(9):1863-9. [PubMed 17385194]*
23. *Dueñas-González A, Zarbá JJ, Patel F, et al, "Phase III, Open-Label, Randomized Study Comparing Concurrent Gemcitabine Plus Cisplatin and Radiation Followed by Adjuvant Gemcitabine and Cisplatin versus Concurrent Cisplatin and Radiation in Patients With Stage IIB to IVA Carcinoma of the Cervix," J Clin Oncol, 2011, 29(13):1678-85. [PubMed 21444871]*
24. *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]*
25. *Edelman MJ, Belani CP, Socinski MA, et al, "Outcomes Associated With Brain Metastases in a Three-Arm Phase III Trial of Gemcitabine-Containing Regimens Versus Paclitaxel Plus Carboplatin for Advanced Non-Small Cell Lung Cancer," J Thorac Oncol, 2010, 5(1):110-6. [PubMed 20035187]*
26. *Fidias PM, Dakhill SR, Lyss AP, et al, "Phase III Study of Immediate Compared With Delayed Docetaxel After Front-Line Therapy With Gemcitabine Plus Carboplatin in Advanced Non-Small-Cell Lung Cancer," J Clin Oncol, 2009, 27(4):591-8. [PubMed 19075278]*
27. *Floyd J, Mirza I, Sachs B, et al, "Hepatotoxicity of Chemotherapy," Semin Oncol, 2006, 33(1):50-67. [PubMed 16473644]*
28. *Gemcitabine [prescribing information]. Lake Forest, IL: Hospira, Inc; May 2014.*
29. *Gemzar (gemcitabine) [prescribing information]. Indianapolis, IN: Lilly; May 2014.*
30. *Gopal AK, Press OW, Shustov AR, et al. Efficacy and safety of gemcitabine, carboplatin, dexamethasone, and rituximab in patients with relapsed/refractory lymphoma: a prospective multi-center phase II study by the Puget Sound Oncology Consortium. Leuk Lymphoma. 2010;51(8):1523-1529. [PubMed 20578815]*
31. *Greco FA, Spigel DR, Kuzur ME, et al. Paclitaxel/carboplatin/gemcitabine versus gemcitabine/vinorelbine in advanced non-small-cell lung cancer: a phase II/III study of the Minnie Pearl Cancer Research Network. Clin Lung Cancer. 2007;8(8):483-437. [PubMed 17922972]*
32. *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]

33. Grønberg BH, Bremnes RM, Flotten O, et al, "Phase III Study by the Norwegian Lung Cancer Study Group: Pemetrexed Plus Carboplatin Compared With Gemcitabine Plus Carboplatin as First-Line Chemotherapy in Advanced Non-Small-Cell Lung Cancer," J Clin Oncol, 2009, 27(19):3217-24. [PubMed 19433683]

34. Heinemann V, Quietzsch D, Gieseler F, et al, "Randomized Phase III Trial of Gemcitabine Plus Cisplatin Compared With Gemcitabine Alone in Advanced Pancreatic Cancer," J Clin Oncol, 2006, 24(24):3946-52. [PubMed 16921047]

35. Helbekkmo N, Sundstrøm SH, Aasebø U, et al, "Vinorelbine/Carboplatin vs Gemcitabine/Carboplatin in Advanced NSCLC Shows Similar Efficacy, But Different Impact of Toxicity," Br J Cancer, 2007, 97(3):283-9.

36. Hensley ML, Blessing JA, Degeest K, et al, "Fixed-Dose Rate Gemcitabine Plus Docetaxel as Second-Line Therapy for Metastatic Uterine Leiomyosarcoma: A Gynecologic Oncology Group Phase II Study," Gynecol Oncol, 2008, 109(3):323-8. [PubMed 18394689]

37. Herman JM, Fan KY, Wild AT, et al. Phase 2 study of erlotinib combined with adjuvant chemoradiation and chemotherapy in patients with resectable pancreatic cancer. Int J Radiat Oncol Biol Phys. 2013;86(4):678-685. [PubMed 23773391]

38. 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]

39. Khorana AA, Mangu PB, Berlin J, et al. Potentially Curable Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2017 Apr 11:JCO2017724948. [PubMed 28398845]

40. 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]

41. Ko AH, Dito E, Schillinger B, et al, "Phase II Study of Fixed Dose Rate Gemcitabine With Cisplatin for Metastatic Adenocarcinoma of the Pancreas," J Clin Oncol, 2006, 24(3):379-85. [PubMed 16344320]

42. Kollmannsberger C, Beyer J, Liersch R, et al, "Combination Chemotherapy With Gemcitabine Plus Oxaliplatin in Patients With Intensively Pretreated or Refractory Germ Cell Cancer: A Study of the German Testicular Cancer Study Group," J Clin Oncol, 2004, 22(1):108-14. [PubMed 14701772]

43. Kuenen BC, Rosen L, Smit EF, et al. Dose-finding and pharmacokinetic study of cisplatin, gemcitabine, and SU5416 in patients with solid tumors. J Clin Oncol. 2002;20(6):1657-1667. [PubMed 11896117]

44. Leu KM, Ostruszka LJ, Shewach D, et al, "Laboratory and Clinical Evidence of Synergistic Cytotoxicity of Sequential Treatment With Gemcitabine Followed by Docetaxel in the Treatment of Sarcoma," J Clin Oncol, 2004, 22(9):1706-12. [PubMed 15117993]

45. Li YF, Fu S, Hu W, et al, "Systemic Anticancer Therapy in Gynecological Cancer Patients With Renal Dysfunction," Int J Gynecol Cancer, 2007, 7(4):739-63. [PubMed 17309673]

46. Look KY, Sandler A, Blessing JA, et al, "Phase II Trial of Gemcitabine as Second-Line Chemotherapy of Uterine Leiomyosarcoma: A Gynecologic Oncology Group (GOG) Study," Gynecol Oncol, 2004, 92(2):644-7. [PubMed 14766260]

47. López A, Gutiérrez A, Palacios A, et al, "GEMOX-R Regimen is a Highly Effective Salvage Regimen in Patients With Refractory/Relapsing Diffuse Large-Cell Lymphoma: A Phase II Study," Eur J Haematol, 2008, 80(2):127-32. [PubMed 18005385]

48. Louvet C, Labianca R, Hammel P, et al, "Gemcitabine in Combination With Oxaliplatin Compared With Gemcitabine Alone in Locally Advanced or Metastatic Pancreatic Cancer: Results of a GERCOR and GISCAD Phase III Trial," J Clin Oncol, 2005, 23(15):3509-16. [PubMed 15908661]

49. Maki RG, Wathen JK, Patel SR, et al, "Randomized Phase II Study of Gemcitabine and Docetaxel Compared With Gemcitabine Alone in Patients With Metastatic Soft Tissue Sarcomas: Results of Sarcoma Alliance for Research Through Collaboration Study 002," J Clin Oncol, 2007, 25(19):2755-63. [PubMed 17602081]

50. Masters GA, Declerck L, Blanke C, et al, "Phase II Trial of Gemcitabine in Refractory or Relapsed Small-Cell Lung Cancer: Eastern Cooperative Oncology Group Trial 1597," J Clin Oncol, 2003, 21(8):1550-5. [PubMed 12697880]

51. Masters GA, Temin S, Azzoli CG. Systemic therapy for stage IV non-small-cell lung cancer: American Society of Clinical Oncology clinical practice guideline update [published correction appears in J Clin Oncol. 2016;34(11):1287]. J Clin Oncol. 2015;33(30):3488-3515 [PubMed 26324367]

52. Merimsky O, Meller I, Flusser G, et al, "Gemcitabine in Soft Tissue or Bone Sarcoma Resistant to Standard

Chemotherapy: A Phase II Study," Cancer Chemother Pharmacol, 2000, 45(2):177-81. [PubMed 10663634]

53. *Monk BJ, Sill MW, McMeekin DS, et al, "Phase III Trial of Four Cisplatin-Containing Doublet Combinations in Stage IVB, Recurrent, or Persistent Cervical Carcinoma: A Gynecologic Oncology Group Study," J Clin Oncol, 2009, 27(28):4649-55. [PubMed 19720909]*
54. *Moore MJ, Goldstein D, Hamm J, et al, "Erlotinib Plus Gemcitabine Compared With Gemcitabine Alone in Patients With Advanced Pancreatic Cancer: A Phase III Trial of the National Cancer Institute of Canada Clinical Trials Group," J Clin Oncol, 2007, 25(15):1960-6. [PubMed 17452677]*
55. *Morgan C, Tillett T, Braybrooke J, et al, "Management of Uncommon Chemotherapy-Induced Emergencies," Lancet Oncol, 2011, 12(8):806-14. [PubMed 21276754]*
56. *Mutch DG, Orlando M, Goss T, et al, "Randomized Phase III Trial of Gemcitabine Compared With Pegylated Liposomal Doxorubicin in Patients With Platinum-Resistant Ovarian Cancer," J Clin Oncol, 2007, 25(19):2811-8. [PubMed 17602086]*
57. *Navid F, Willert JR, McCarville MB, et al, "Combination of Gemcitabine and Docetaxel in the Treatment of Children and Young Adults With Refractory Bone Sarcoma," Cancer, 2008, 113(2):419-25. [PubMed 18484657]*
58. *Neoptolemos JP, Palmer DH, et al; European Study Group for Pancreatic Cancer. 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]*
59. *Nishijima Y, Hirata H, Himeno A, et al. Drug-induced thrombotic thrombocytopenic purpura successfully treated with recombinant human soluble thrombomodulin [published online May 15, 2013].Intern Med. 2013;52(10):1111-1114. [PubMed 23676600]*
60. *Nowak AK, Byrne MJ, Williamson R, et al, "A Multicentre Phase II Study of Cisplatin and Gemcitabine for Malignant Mesothelioma," Br J Cancer, 2002, 87(5):491-6. [PubMed 12189542]*
61. *Palmieri G, Merola G, Federico P, et al, "Preliminary Results of Phase II Study of Capecitabine and Gemcitabine (CAP-GEM) in Patients With Metastatic Pretreated Thymic Epithelial Tumors (TETs)," Ann Oncol, 2010, 21(6):1168-72. [PubMed 19880439]*
62. *Park YH, Jung KH, Im SA, et al. Phase III, multicenter, randomized trial of maintenance chemotherapy versus observation in patients with metastatic breast cancer after achieving disease control with six cycles of gemcitabine plus paclitaxel as first-line chemotherapy: KCSG-BR07-02. J Clin Oncol. 2013;31(14):1732-9. [PubMed 23569309]*
63. *Pectasides D, Pectasides M, Farmakis D, et al, "Gemcitabine and Oxaliplatin (GEMOX) in Patients With Cisplatin-Refractory Germ Cell Tumors: A Phase II Study," Ann Oncol, 2004, 15(3):493-7. [PubMed 14998855]*
64. *Pfisterer J, Vergote I, Du Bois A, et al, "Combination Therapy with Gemcitabine and Carboplatin in Recurrent Ovarian Cancer," Int J Gynecol Cancer, 2005, 15 (Suppl 1):36-41. [PubMed 15839957]*
65. *Poplin E, Feng Y, Berlin J, et al, "Phase III, Randomized Study of Gemcitabine and Oxaliplatin Versus Gemcitabine (Fixed-Dose Rate Infusion) Compared With Gemcitabine (30-Minute Infusion) in Patients With Pancreatic Carcinoma E6201: a Trial of the Eastern Cooperative Oncology Group," J Clin Oncol, 2009, 27(23):3778-85. [PubMed 19581537]*
66. *Pouessel D, Culine S, Becht C, et al, "Gemcitabine and Docetaxel as Front-Line Chemotherapy in Patients With Carcinoma of an Unknown Primary Site," Cancer, 2004, 100(6):1257-61. [PubMed 15022294]*
67. *Pujol JL, Breton JL, Gervais R, et al. Gemcitabine-docetaxel versus cisplatin-vinorelbine in advanced or metastatic non-small-cell lung cancer: a phase III study addressing the case for cisplatin. Ann Oncol. 2005;16(4):602-610. [PubMed 15741225]*
68. *Santoro A, Magagnoli M, Spina M, et al, "Ifosfamide, Gemcitabine, and Vinorelbine: A New Induction Regimen for Refractory and Relapsed Hodgkin's Lymphoma," Haematologica, 2007, 92(1):35-41. [PubMed 17229633]*
69. *Schilder RJ, Blessing J, and Cohn DE, "Evaluation of Gemcitabine in Previously Treated Patients With Non-Squamous Cell Carcinoma of the Cervix: A Phase II Study of the Gynecologic Oncology Group," Gynecol Oncol, 2005, 96(1):103-7. [PubMed 15589587]*
70. *Seliger G, Mueller LP, Kegel T, et al, "Phase 2 Trial of Docetaxel, Gemcitabine, and Oxaliplatin Combination Chemotherapy in Platinum- and Paclitaxel-Pretreated Epithelial Ovarian Cancer," Int J Gynecol Cancer, 2009, 19(8):1446-53. [PubMed 20009905]*
71. *Tannir NM, Thall PF, Ng CS, et al, "A Phase II Trial of Gemcitabine Plus Capecitabine for Metastatic Renal Cell Cancer Previously Treated With Immunotherapy and Targeted Agents," J Urol, 2008, 180(3):867-72. [PubMed 18635226]*

72. *Tempero M, Plunkett W, Ruiz Van Haperen V, "Randomized Phase II Comparison of Dose-Intense Gemcitabine: Thirty-Minute Infusion and Fixed Dose Rate Infusion in Patients With Pancreatic Adenocarcinoma," J Clin Oncol, 2003, 21(18):3402-8. [PubMed 12885837]*

73. *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.*

74. *Valle J, Wason H, Palmer DH, et al, "Cisplatin Plus Gemcitabine Versus Gemcitabine for Biliary Tract Cancer," N Engl J Med, 2010 362(14):1273-81. [PubMed 20375404]*

75. *van Haarst JM, Baas P, Manegold Ch, et al, "Multicentre Phase II Study of Gemcitabine and Cisplatin in Malignant Pleural Mesothelioma," Br J Cancer, 2002, 86(3):342-5. [PubMed 11875695]*

76. *Venook AP, Egorin MJ, Rosner GL, et al, "Phase I and Pharmacokinetic Trial of Gemcitabine in Patients With Hepatic or Renal Dysfunction: Cancer and Leukemia Group B 9565," J Clin Oncol, 2000, 18(14):2780-7. [PubMed 10894879]*

77. *von der Maase H, Hansen SW, Roberts JT, et al, "Gemcitabine and Cisplatin Versus Methotrexate, Vinblastine, Doxorubicin, and Cisplatin in Advanced or Metastatic Bladder Cancer: Results of a Large, Randomized, Multinational, Multicenter, Phase III Study," J Clin Oncol, 2000, 18(17):3068-77. [PubMed 11001674]*

78. *Von Hoff DD, Ervin TJ, Arena FP, et al. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. N Engl J Med. 2013;369(18):1691-1703. [PubMed 24131140]*

79. *Waters JS, Moss C, Puyle L, et al, "Phase II Clinical Trial of Capecitabine and Gemcitabine Chemotherapy in Patients With Metastatic Renal Carcinoma," Br J Cancer, 2004, 91(10):1763-8. [PubMed 15505625]*

80. *Xenidis N, Chelis L, Amarantidis K, et al. Docetaxel plus gemcitabine in combination with capecitabine as treatment for inoperable pancreatic cancer: a phase II study. Cancer Chemother Pharmacol. 2012;69(2):477-484. [PubMed 21858532]*

81. *Zhang L, Zhang Y, Huang PY, et al, "Phase II Clinical Study of Gemcitabine in the Treatment of Patients With Advanced Nasopharyngeal Carcinoma After the Failure of Platinum-Based Chemotherapy," Cancer Chemother Pharmacol, 2008, 61(1):33-8. [PubMed 17909810]*

82. *Zupancic M, Shah PC, Shah-Khan F. Gemcitabine-associated thrombotic thrombocytopenic purpura. Lancet Oncol. 2007;8(7):634-641. [PubMed 17613425]*

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