

Gemcitabine

Class:

Antineoplastic Agent, Antimetabolite (Pyrimidine Analog)

Indications:

Breast cancer
Non small cell lung cancer
Ovarian cancer
Pancreatic cancer

Unlabeled use:

Bladder cancer
Cervical cancer
Head and neck cancer
Hepatobiliary cancer
Hodgkin lymphoma
Malignant pleural mesothelioma
Non-Hodgkin lymphoma
Sarcoma
Small cell lung cancer
Testicular cancer
Unknown-primary, adenocarcinoma
Uterine cancer

Available dosage form in the hospital:

200 mg VIAL
1gVIAL

Trade Names:

Gemzar

Doses: Details concerning dosing in combination regimens should also be consulted. **Note:** Prolongation of the infusion duration >60 minutes and administration more frequently than once weekly have been shown to increase toxicity.

- Breast cancer, metastatic:** I.V.: 1250 mg/m² over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with paclitaxel) **or** (unlabeled dosing; as a single agent) 800 mg/m² 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:** I.V.: 1000 mg/m² over 30 minutes days 1, 8, and 15; repeat cycle every 28 days (in combination with cisplatin) **or** 1250 mg/m² over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with cisplatin) **or** (unlabeled dosing/combination) 1000 mg/m² over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with carboplatin) for up to 4 cycles.
- Ovarian cancer, advanced:** I.V.: 1000 mg/m² over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with carboplatin) **or** (unlabeled dosing; as a single agent) 1000 mg/m² over 30-60 minutes days 1 and 8; repeat cycle every 21 days
- Pancreatic cancer, locally advanced or metastatic:** I.V.: Initial: 1000 mg/m² 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** (unlabeled combinations) 1000 mg/m² 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) **or** 1000 mg/m² over 30 minutes days 1, 8, and 15 every 28 days (in combination with capecitabine) **or** 1000 mg/m² over 30 minutes days 1 and 15 every 28 days (in combination with cisplatin) (Heinemann,

- 2006) **or** 1000 mg/m² infused at 10 mg/m²/minute every 14 days (in combination with oxaliplatin) **or** 1000 mg/m² days 1, 8, and 15 every 28 days (in combination with paclitaxel [protein bound])
- Bladder cancer (unlabeled use):**
- Advanced or metastatic:* I.V.: 1000 mg/m² over 30-60 minutes days 1, 8, and 15; repeat cycle every 28 days (in combination with cisplatin)
 - Transitional cell carcinoma:* Intravascular 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
- Cervical cancer, recurrent or persistent (unlabeled use):** I.V.: 1000 mg/m² days 1 and 8; repeat cycle every 21 days (in combination with cisplatin) **or** 1250 mg/m² over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with cisplatin) **or** 800 mg/m² over 30 minutes days 1, 8, and 15; repeat cycle every 28 days (as a single-agent) **or** 800 mg/m² days 1 and 8; repeat cycle every 28 days (in combination with cisplatin)
- Head and neck cancer, nasopharyngeal (unlabeled use):** I.V.: 1000 mg/m² over 30 minutes days 1, 8, and 15 every 28 days **or** 1000 mg/m² over 30 minutes days 1 and 8 every 21 days (in combination with vinorelbine)
- Hepatobiliary cancer, advanced (unlabeled use):** I.V.: 1000 mg/m² over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with cisplatin) (Valle, 2010) **or** 1000 mg/m² over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with capecitabine) (Knox, 2005) **or** 1000 mg/m² infused at 10 mg/m²/minute every 2 weeks (in combination with oxaliplatin)
- Hodgkin lymphoma, relapsed (unlabeled use):** I.V.: 1000 mg/m² (800 mg/m² 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/m² days 1 and 4; repeat cycle every 21 days (in combination with ifosfamide, mesna, vinorelbine, and prednisolone)
- Malignant pleural mesothelioma (unlabeled use; in combination with cisplatin):** I.V.: 1000 mg/m² over 30 minutes days 1, 8 and 15 every 28 days for up to 6 cycles (Nowak, 2002) **or** 1250 mg/m² over 30 minutes days 1 and 8 every 21 days for up to 6 cycles.
- Non-Hodgkin lymphoma, refractory (unlabeled use):** I.V.: 1000 mg/m² over 30 minutes days 1 and 8; repeat cycle every 21 days (in combination with cisplatin and dexamethasone) (Crump, 2004) **or** 1000 mg/m² every 15-21 days (in combination with oxaliplatin and rituximab)
- Sarcoma (unlabeled uses):** I.V.:
- Ewing's sarcoma, refractory: 675 mg/m² over 90 minutes days 1 and 8; repeat cycle every 21 days (in combination with Docetaxel)
 - Osteosarcoma, refractory: 675 mg/m² over 90 minutes days 1 and 8; repeat cycle every 21 days (in combination with Docetaxel) **or** 1000 mg/m² weekly for 7 weeks followed by 1 week rest; then weekly for 3 weeks out of every 4 weeks
 - Soft tissue sarcoma, advanced: 800 mg/m² over 90 minutes days 1 and 8; repeat cycle every 21 days (in combination with vinorelbine) **or** 675 mg/m² over 90 minutes days 1 and 8; repeat cycle every 21 days (in combination with Docetaxel) **or** 900 mg/m² 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 (unlabeled use):** I.V.: 1000-1250 mg/m² over 30 minutes days 1, 8, and 15 every 28 days (as a single agent) (Masters, 2003)
- Testicular cancer, refractory germ cell (unlabeled use):** I.V.: 1000-1250 mg/m² over 30 minutes days 1 and 8 every 21 days (in combination with oxaliplatin) **or** 1000 mg/m² 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/m² over 30 minutes days 1 and 8 every 21 days (in combination with oxaliplatin and paclitaxel)
- Unknown-primary, adenocarcinoma (unlabeled use):** I.V.: 1250 mg/m² days 1 and 8 every 21 days (in combination with cisplatin) **or** 1000 mg/m² over 30 minutes days 1 and 8 every 21 days for up to 6 cycles (in combination with Docetaxel)
- Uterine cancer (unlabeled use):** I.V.: 900 mg/m² over 90 minutes days 1 and 8 every 21 days (in combination with Docetaxel) (Hensley, 2008) **or** 1000 mg/m² over 30 minutes days 1, 8, and 15 every 28 days (Look, 2004).

Geriatric

Refer to adult dosing

Renal Impairment:

-No dosage adjustment provided in 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 6-12 hours after gemcitabine infusion (Janus 2010; Li, 2007).

Hepatic Impairment:

- No dosage adjustment provided in 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/m²; 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)

****Hematologic toxicity:**

1. Breast cancer:

Day 1:

- Absolute granulocyte count (AGC) $\geq 1500/\text{mm}^3$ and platelet count $\geq 100,000/\text{mm}^3$: Administer 100% of full dose

-AGC $< 1500/\text{mm}^3$ or platelet count $< 100,000/\text{mm}^3$: Hold dose

Day 8:

- AGC $\geq 1200/\text{mm}^3$ and platelet count $> 75,000/\text{mm}^3$: Administer 100% of full dose
- AGC 1000-1199/ mm^3 or platelet count 50,000-75,000/ mm^3 : Administer 75% of full dose
- AGC 700-999/ mm^3 and platelet count $\geq 50,000/\text{mm}^3$: Administer 50% of full dose
- AGC $< 700/\text{mm}^3$ or platelet count $< 50,000/\text{mm}^3$: Hold dose

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

- AGC $\geq 1000/\text{mm}^3$ and platelet count $\geq 100,000/\text{mm}^3$: Administer 100% of full dose
- AGC 500-999/ mm^3 or platelet count 50,000-99,999/ mm^3 : Administer 75% of full dose
- AGC $< 500/\text{mm}^3$ or platelet count $< 50,000/\text{mm}^3$: Hold dose

3. Ovarian cancer:

- Day 1:

- AGC $\geq 1500/\text{mm}^3$ and platelet count $\geq 100,000/\text{mm}^3$: Administer 100% of full dose
- AGC $< 1500/\text{mm}^3$ or platelet count $< 100,000/\text{mm}^3$: Delay treatment cycle

- Day 8:

- AGC $\geq 1500/\text{mm}^3$ and platelet count $\geq 100,000/\text{mm}^3$: Administer 100% of full dose

- AGC 1000-1499/mm³ or platelet count 75,000-99,999/mm³: Administer 50% of full dose
- AGC <1000/mm³ or platelet count <75,000/mm³: Hold dose

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

- Initial occurrence: AGC <500/mm³ for >5 days, AGC <100/mm³ for >3 days, febrile neutropenia, platelet count <25,000/mm³, or cycle delay >1 week due to toxicity: Permanently reduce gemcitabine to 800 mg/m² on days 1 and 8.
- Subsequent occurrence: AGC <500/mm³ for >5 days, AGC <100/mm³ for >3 days, neutropenic fever, platelet count <25,000/mm³, or cycle delay >1 week due to toxicity: Permanently reduce gemcitabine to 800 mg/m² and administer on day 1 only.

4. Pancreatic cancer:

- AGC ≥1000/mm³ and platelet count ≥100,000/mm³: Administer 100% of full dose
- AGC 500-999/mm³ or platelet count 50,000-99,999/mm³: Administer 75% of full dose
- AGC <500/mm³ or platelet count <50,000/mm³: Hold dose

Common side effect:

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

Central nervous system: Drowsiness (11%)

Dermatologic: Skin rash (28% to 30%), alopecia (15% to 16%), pruritus (13%)

Gastrointestinal: Nausea/vomiting (69% to 71%), diarrhea (19% to 30%), stomatitis (10% to 11%)

Genitourinary: Proteinuria (32% to 45%), hematuria (23% to 35%), increased blood urea nitrogen (15% to 16%)

Hematologic & oncologic: Anemia (68% to 73%; grade 4: 1% to 3%), leukopenia (62% to 64%; grade 4: ≤1%), neutropenia (61% to 63%; grade 4: 6% to 7%), thrombocytopenia (24% to 36%; grade 4: 1%), hemorrhage (4% to 17%; grade 3: <1%; grade 4: <1%); bone marrow depression is the dose-limiting toxicity

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

Infection: Localized infection (10% to 16%)

Respiratory: Dyspnea (10% to 23%; grade 3: 3%; grade 4: <1%)

Miscellaneous: Fever (16% to 41%), flu-like symptoms (19%)

Pregnancy Risk Factor: D