VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

Gemzar (gemcitabine)

Effective Date: 1/31/12
Date Developed: 12/14/11 by Albert Reeves MD
Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19, 2/18/20, 8/3/21, 2/1/22

Gemcitabine is an Antineoplastic Agent; Antimetabolite. Gemcitabine is a pyrimidine antimetabolite that inhibits DNA synthesis by inhibition of DNA polymerase and ribonucleotide reductase.

Pre-Authorization Criteria:

Breast cancer: First-line treatment of metastatic breast cancer (in combination with paclitaxel) after failure of adjuvant chemotherapy which contained an anthracycline, e.g. doxyrubicin (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: First-line treatment of locally-advanced (nonresectable stage II or III) or metastatic (stage IV) pancreatic adenocarcinoma

NOTE: VCHCP requires that Gemcitabine be prescribed by an Oncologist.

Dosing: Adult

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

Pancreatic cancer, locally advanced or metastatic: I.V.: Initial: 1000 mg/m^2 over 30 minutes

once weekly for up to 7 weeks followed by 1 week rest; then once weekly for 3 weeks out of every 4 weeks

Dose escalation: Patients who complete an entire cycle of therapy may have the dose in subsequent cycles increased by 25% as long as the absolute granulocyte count (AGC) nadir is >1500/mm^3, platelet nadir is >100,000/mm^3, and nonhematologic toxicity is less than WHO Grade 1. If the increased dose is

tolerated (with the same parameters) the dose in subsequent cycles may again be increased by 20%.

Pancreatic cancer, advanced (unlabeled dosing/combinations): I.V.: 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 4 weeks (in combination with capecitabine) (Cunningham, 2009) **or** 1000 mg/m^2 over 30 minutes days 1 and 15 every 4 weeks (in combination with cisplatin) (Heinemann, 2006) **or** 1000 mg/m^2 infused at 10 mg/m^2/minute every 2 weeks (in combination with oxaliplatin) (Louvet, 2005)

Nonsmall cell lung cancer, locally advanced or metastatic (in combination with cisplatin): I.V.: 1000 mg/m^2 over 30 minutes days 1, 8, and 15; repeat cycle
every 28 days **or** 1250 mg/m^2 over 30 minutes days 1 and 8; repeat cycle every
21 days

Breast cancer, metastatic (AGC should be ≥1500/mm^3 and platelets ≥100,000/mm^3 prior to each cycle): I.V.: 1250 mg/m^2 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/m^2 over 30 minutes days 1, 8, and 15 of a 28- day treatment cycle (Carmichael, 1995)

Ovarian cancer, advanced (AGC should be ≥1500/mm^3 and platelets ≥100,000/mm^3 prior to each cycle): I.V.: 1000 mg/m^2 over 30 minutes days 1 and 8; repeat

cycle every 21 days (in combination with carboplatin)

OFF-LABEL USES:

Biliary tract cancer, advanced (unlabeled use): I.V.: 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 over 100 minutes every 2 weeks (in combination with oxaliplatin) (Andre, 2004)

Bladder cancer (unlabeled use):

Advanced or metastatic: I.V.: 1000 mg/m^2 over 30-60 minutes days 1, 8, and 15; repeat cycle every 4 weeks (in combination with cisplatin) (von der Maase, 2000)

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 (unlabeled use): I.V.: 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)

Head and neck cancer, nasopharyngeal (unlabeled use): I.V.: 1000 mg/m^2 over 30 minutes days 1, 8, and 15 every 4 weeks (Zhang, 2008)

Hodgkin lymphoma, relapsed (unlabeled use): I.V.: 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 (unlabeled use; in combination with cisplatin): I.V.: 1000 mg/m^2 over 30 minutes days 1, 8 and 15 every 4 weeks for up to 6 cycles (Nowak, 2002) **or** 1250 mg/m^2 over 30 minutes days 1 and 8 every 3 weeks for up to 6 cycles (van Haarst, 2002)

Non-Hodgkin lymphoma, refractory (unlabeled use): I.V.: 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 15-21days (in combination with oxaliplatin and rituximab) (Lopez, 2008)

Sarcoma (unlabeled uses): I.V.:

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: I.V.: 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 (unlabeled use): I.V.: 1000- 1250 mg/m^2 over

30 minutes days 1, 8, and 15 every 4 weeks (as a single agent)
(Masters, 2003)

Testicular cancer, refractory germ cell (unlabeled use): I.V.: 1000 mg/m^2 over 30 minutes days 1 and 8 every 3 weeks (in combination with oxaliplatin) (Kohllmannsberger, 2004; Pectasides, 2004) **or** 1250 mg/m^2 over 30 minutes days 1 and 8 every 3 weeks (in combination with oxaliplatin) (De Giorgi, 2006) **or** 1000 mg/m^2 over 30 minutes days 1, 8 and 15 every 4 weeks for up to 6 cycles (in combination with paclitaxel) (Hinton, 2002)

Unknown-primary, adenocarcinoma (unlabeled use): I.V.: 1250 mg/m^2 days 1 and 8 every 3 weeks (in combination with cisplatin) (Culine, 2003) **or** 1000 mg/m^2 over 30 minutes days 1 and 8 every 3 weeks (in combination with docetaxel) for up to 6 cycles (Pouessel, 2004)

Uterine cancer (unlabeled use): I.V.: 900 mg/m^2 over 90 minutes days 1 and 8 every 3 weeks (in combination with docetaxel) (Hensley, 2008) **or** 1000 mg/m^2 over 30 minutes days 1, 8, and 15 every 4 weeks (Look, 2004)

Dosing: Pediatric

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

Details concerning dosing in combination regimens should also be consulted. **Note**: Prolongation of the infusion time >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 (unlabeled use): I.V.: 1000 mg/m^2 over 30 minutes days 1, 8, and 15 every 4 weeks (in combination with paclitaxel) for up to 6 cycles (Hinton, 2002)

Hodgkin lymphoma, relapsed (unlabeled use): I.V.: 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 (unlabeled use): I.V.:

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.

Dosage Forms: U.S.

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

Injection, powder for reconstitution: 200 mg, 1 g, 2 g

Gemzar®: 200 mg, 1 g

Injection, solution: 38 mg/mL (5.26 mL, 26.3 mL, 52.6 mL)

Administration

Infuse over 30 minutes; for unlabeled 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 (unlabeled); prolonged infusion times increase the accumulation of the active

metabolite, gemcitabine triphosphate, optimizing the pharmacokinetics (Ko, 2006; Tempero, 2003). Patients who receive gemcitabine FDR experience more grade 3/4 hematologic toxicity (Ko, 2006; Poplin, 2009).

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

WARNINGS / PRECAUTIONS

Concerns related to adverse effects:

Bone marrow suppression: May cause bone marrow suppression (leukopenia, thrombocytopenia, and anemia); myelosuppression is generally the dose-limiting toxicity. Monitor blood counts; dosage adjustments are frequently required.

Fever: May cause fever in the absence of clinical infection.

Hemolytic uremic syndrome: Hemolytic uremic syndrome (and/or renal failure) has been reported; monitor for evidence of microangiopathic hemolysis (elevation of bilirubin or LDH, reticulocytosis, severe thrombocytopenia, and/or renal failure).

Hepatotoxicity: Serious hepatotoxicity (including liver failure and death) has been reported (when alone or used in combination with other hepatotoxic medications); use with caution in patients with hepatic impairment (history of cirrhosis, hepatitis, or alcoholism) or in patients with hepatic metastases; may lead to exacerbation of hepatic impairment. Dose adjustments may be considered with elevated bilirubin.

Pulmonary toxicity: Pulmonary toxicity has been observed; discontinue if severe and institute supportive measures.

Disease-related concerns:

Renal impairment: Use with caution in patients with pre-existing renal impairment.

DRUG Interactions

(For additional information: Launch Lexi-Interact™ Drug Interactions Program)

BCG: Immunosuppressants may diminish the therapeutic effect of BCG. *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*

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

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

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

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

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*

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

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

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*

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

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). *Risk C: Monitor therapy*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Vaccinial infections may develop. 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): Antineoplastic Agents may enhance the anticoagulant effect of Vitamin K Antagonists. Antineoplastic Agents may diminish the anticoagulant effect of Vitamin K Antagonists. *Risk C: Monitor therapy*

Dosage Forms:

200 mg/5.26 mL (5.26 mL); 200 mg/2 mL (2 mL); 1 g/10 mL (10 mL); 1 g/26.3 mL (26.3 mL); 1.5 g/15 mL (15 mL); 2 g/20 mL (20 mL); 2 g/52.6 mL (52.6 mL)

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