Reference number(s)
4469-A

STANDARD MEDICARE PART B MANAGEMENT

GEMZAR (gemcitabine)
INFUGEM (gemcitabine in sodium chloride injection)
gemcitabine

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Ovarian cancer
   In combination with carboplatin for the treatment of patients with advanced ovarian cancer that has relapsed at least 6 months after completion of platinum-based therapy
2. Breast cancer
   In combination with paclitaxel for the first-line treatment of patients with metastatic breast cancer after failure of prior anthracycline-containing adjuvant chemotherapy, unless anthracyclines were clinically contraindicated
3. Non-small cell lung cancer
   In combination with cisplatin for the first-line treatment of patients with inoperable, locally advanced (Stage IIIA or IIIB) or metastatic (Stage IV) non-small cell lung cancer (NSCLC)
4. Pancreatic cancer
   As first-line treatment for patients with locally advanced (nonresectable Stage II or Stage III) or metastatic (Stage IV) adenocarcinoma of the pancreas. Gemzar, Infugem and gemcitabine are indicated for patients previously treated with fluorouracil.

B. Compendial Uses

1. Ampullary adenocarcinoma
2. Bladder cancer, primary carcinoma of the urethra, upper genitourinary tract tumors, transitional cell carcinoma of the urinary tract, urothelial carcinoma of the prostate, non-urothelial and urothelial cancer with variant histology
3. Bone cancer
   i. Ewing's sarcoma
   ii. Mesenchymal chondrosarcoma
   iii. Osteosarcoma
   iv. Dedifferentiated chondrosarcoma
   v. High-grade undifferentiated pleomorphic sarcoma (UPS)
4. Breast cancer
5. Head and neck cancers (including very advanced head and neck cancer, cancer of the nasopharynx, and salivary gland tumors)
6. Hepatocellular carcinoma
7. Hepatobiliary and biliary tract cancers

   i. Extrahepatic cholangiocarcinoma
   ii. Intrahepatic cholangiocarcinoma
   iii. Gallbladder cancer
8. Hodgkin lymphoma
   i. Classic Hodgkin lymphoma
   ii. Nodular lymphocyte-predominant Hodgkin lymphoma
   iii. Pediatric Hodgkin lymphoma
9. Kidney cancer
10. Malignant pleural or peritoneal mesothelioma
11. Non-small cell lung cancer (NSCLC)
12. Occult primary tumors (cancer of unknown primary)
13. Ovarian cancer, fallopian tube cancer, and primary peritoneal cancer
14. Malignant germ cell tumors
15. Pancreatic adenocarcinoma
16. Small cell lung cancer (SCLC)
17. Soft tissue sarcoma
   i. Angiosarcoma
   ii. Extremity/Body wall, head/neck
   iii. Retroperitoneal/intra-abdominal
   iv. Rhabdomyosarcoma
   v. Solitary fibrous tumor
   vi. Dermatofibrosarcoma protuberans (DFSP) with fibrosarcomatous transformation
18. Testicular cancer
19. Thymomas and thymic carcinomas
20. Uterine neoplasms (including uterine sarcoma and uterine leiomyosarcoma)
21. Kaposi sarcoma
22. Primary cutaneous lymphomas
   i. Mycosis fungoides/Sezary syndrome
   ii. Primary cutaneous CD30+ T-cell lymphoproliferative disorders
23. T-cell lymphomas
   i. Peripheral T-cell lymphomas
   ii. Adult T-cell leukemia/lymphoma
   iii. Extranodal natural killer (NK)/T-cell lymphoma
   iv. Hepatosplenic T-cell lymphoma
   v. Breast implant-associated anaplastic large cell lymphoma (ALCL)
24. Gestational trophoblastic neoplasia
25. B-Cell lymphomas
   i. Follicular lymphoma (grade 1-2)
   ii. Histologic transformation of indolent lymphoma to diffuse large B-cell lymphoma
   iii. Mantle cell lymphoma
   iv. Diffuse large B-cell lymphoma
   v. High-grade B-cell lymphomas
   vi. Burkitt lymphoma
   vii. AIDS-related B-cell lymphomas
   viii. Post-transplant lymphoproliferative disorders
26. Cervical cancer
27. Vulvar cancer
28. Small bowel adenocarcinoma

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. CRITERIA FOR INITIAL APPROVAL

A. Pancreatic adenocarcinoma
Authorization of 6 months may be granted for treatment of pancreatic adenocarcinoma.

B. Breast cancer
Authorization of 6 months may be granted for treatment of members with no response to preoperative systemic therapy, advanced, recurrent, or metastatic breast cancer.

C. **Hepatocellular carcinoma**
Authorization of 6 months may be granted for treatment of hepatocellular carcinoma.

D. **Hepatobiliary and biliary tract cancer**
Authorization of 6 months may be granted for treatment of hepatobiliary and biliary tract cancer (including intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, and gallbladder cancer).

E. Ampullary Adenocarcinoma
Authorization of 6 months may be granted for treatment of ampullary adenocarcinoma.

F. Ovarian cancer, fallopian tube cancer, and primary peritoneal cancer
Authorization of 6 months may be granted for treatment of advanced, persistent, relapsed or recurrent disease if the member has one of the following:
1. Epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer
2. Carcinosarcoma (malignant mixed Mullerian tumors)
3. Clear cell carcinoma of the ovary
4. Mucinous carcinoma of the ovary
5. Grade 1 endometroid carcinoma
6. Low-grade serous carcinoma/ovarian borderline epithelial tumors (low malignant potential)
7. Malignant germ cell tumors

G. **Non-small cell lung cancer (NSCLC)**
Authorization of 6 months may be granted for treatment of NSCLC.

H. **Bladder cancer, primary carcinoma of the urethra, upper genitourinary tract tumors, transitional cell carcinoma of the urinary tract, urothelial carcinoma of the prostate, and non-urothelial and urothelial cancer with variant histology**
Authorization of 6 months may be granted for treatment of bladder cancer, primary carcinoma of the urethra, upper genitourinary tract tumors, transitional cell carcinoma of the urinary tract, urothelial carcinoma of the prostate, and non-urothelial and urothelial cancer with variant histology.

I. **Small cell lung cancer (SCLC)**
Authorization of 6 months may be granted for treatment of SCLC.

J. **Soft tissue sarcoma**

Authorization of 6 months may be granted for treatment of soft tissue sarcoma (including angiosarcoma, extremity/body wall, head/neck, retroperitoneal/intra-abdominal, rhabdomyosarcoma, solitary fibrous tumor, and dermatofibrosarcoma protuberans (DFSP) with fibrosarcomatous transformation).

K. **Bone cancer**

1. **Ewing's sarcoma or mesenchymal chondrosarcoma**
   Authorization of 6 months may be granted for treatment of relapsed, progressive, or metastatic Ewing's sarcoma or mesenchymal chondrosarcoma.

2. **Osteosarcoma, dedifferentiated chondrosarcoma, or high-grade undifferentiated pleomorphic sarcoma (UPS)**
   Authorization of 6 months may be granted for treatment of relapsed/refractory or metastatic osteosarcoma, dedifferentiated chondrosarcoma, or high-grade undifferentiated pleomorphic sarcoma (UPS)..

L. **Head and neck cancer**
Authorization of 6 months may be granted for treatment of head and neck cancer (including very advanced head and neck cancer, cancer of the nasopharynx, and salivary gland tumors).

M. **Hodgkin lymphoma**

1. **Hodgkin lymphoma**
   Authorization of 6 months may be granted for treatment of Hodgkin lymphoma including classic Hodgkin lymphoma and pediatric Hodgkin lymphoma.

2. **Nodular lymphocyte-predominant Hodgkin lymphoma**
   Authorization of 6 months may be granted for treatment of progressive, relapsed, or refractory nodular lymphocyte-predominant Hodgkin lymphoma.

N. **Kidney cancer**
Authorization of 6 months may be granted for treatment of unresectable, relapsed, or metastatic kidney cancer.

O. **Malignant pleural or peritoneal mesothelioma**
Authorization of 6 months may be granted for treatment of malignant pleural or peritoneal mesothelioma, including pericardial mesothelioma and tunica vaginalis testis mesothelioma.

P. **Occult primary tumors (cancer of unknown primary)**
Authorization of 6 months may be granted for treatment of occult primary tumors.

Q. **Thymomas and thymic carcinomas**
Authorization of 6 months may be granted for treatment of thymomas and thymic carcinomas.

R. **Testicular cancer**
Authorization of 6 months may be granted for treatment of testicular cancer.

S. **Uterine neoplasms**
Authorization of 6 months may be granted for treatment of uterine neoplasms (including uterine sarcoma and uterine leiomyosarcoma).

T. **Kaposi sarcoma**
Authorization of 6 months may be granted for treatment of Kaposi sarcoma.

U. **Primary cutaneous lymphomas**
Authorization of 6 months may be granted for treatment of primary cutaneous lymphomas (including mycosis fungoides/Sezary syndrome and primary cutaneous CD30+ T-cell lymphoproliferative disorders).

V. **T-cell lymphomas**
Authorization of 6 months may be granted for treatment of T-cell lymphomas (including peripheral T-cell lymphomas, adult T-cell leukemia/lymphoma, hepatosplenic T-cell lymphoma, breast implant-associated anaplastic large cell lymphoma [ALCL], and extranodal NK/T-cell lymphoma).

W. **Gestational trophoblastic neoplasia**
Authorization of 6 months may be granted for treatment of gestational trophoblastic neoplasia.

X. **B-cell lymphomas**
Authorization of 6 months may be granted for treatment of B-cell lymphomas (including follicular lymphoma [grade 1-2], histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma, mantle cell lymphoma, diffuse large B-cell lymphoma, high-grade B-cell lymphomas, Burkitt lymphoma, AIDS-related B-cell lymphomas, and post-transplant lymphoproliferative disorders).

Y. **Cervical cancer**
Authorization of 6 months may be granted for treatment of cervical cancer.

Z. **Vulvar cancer**
Authorization of 6 months may be granted for treatment of vulvar cancer.

AA. **Small bowel adenocarcinoma**
Authorization of 6 months may be granted for treatment of small bowel adenocarcinoma.

BB. Malignant germ cell tumor
Authorization of 6 months may be granted for treatment of malignant germ cell tumor.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

Authorization for 6 months may be granted when all of the following criteria are met:
A. The member is currently receiving therapy with the requested drug
B. The requested drug is being used to treat an indication enumerated in Section II
C. The member is receiving benefit from therapy. Benefit is defined as:
   1. No evidence of unacceptable toxicity while on the current regimen AND
   2. No evidence of disease progression while on the current regimen

IV. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:
1. The prescribing information for Gemzar, Infugem and generic gemcitabine.

2. The available compendium
    a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    b. Micromedex DrugDex
    c. American Hospital Formulary Service- Drug Information (AHFS-DI)
    d. Lexi-Drugs
    e. Clinical Pharmacology
3. NCCN Guideline: Hodgkin lymphoma
4. NCCN Guideline: Thymomas and thymic carcinomas
5. NCCN Guideline: Small Cell Lung Cancer
6. NCCN Guideline: Cervical cancer
7. NCCN Guideline: Gestational trophoblastic neoplasia
8. NCCN Guideline: Small bowel adenocarcinoma
9. NCCN Guideline: Peritoneal mesothelioma
10. NCCN Guideline: Pleural mesothelioma
11. NCCN Guideline: T-cell lymphomas
12. NCCN Guideline: Pediatric Hodgkin lymphoma
13. NCCN Guideline: Kaposi sarcoma
14. NCCN Guideline: Bone cancer
15. NCCN Guideline: Testicular cancer
16. NCCN Guideline: Non-small cell lung cancer
17. NCCN Guideline: Breast cancer
18. NCCN Guideline: Soft tissue sarcoma
19. NCCN Guideline: Occult primary
20. NCCN Guideline: Biliary tract cancers
21. NCCN Guideline: Ampullary adenocarcinoma
22. NCCN Guideline: Bladder cancer
23. NCCN Guideline: B-cell lymphomas
24. NCCN Guideline: Uterine neoplasms
25. NCCN Guideline: Primary cutaneous lymphomas
26. NCCN Guideline: Ovarian cancer/Fallopian tube cancer/primary peritoneal cancer
27. NCCN Guideline: Vulvar cancer
28. NCCN Guideline: Pancreatic adenocarcinoma
29. NCCN Guideline: Head and neck cancers
30. NCCN Guideline: Kidney cancer

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Gemzar, Infugem and generic gemcitabine are covered in addition to the following:

1. Ampullary adenocarcinoma
2. Bladder cancer, primary carcinoma of the urethra, upper genitourinary tract tumors, transitional cell carcinoma of the urinary tract, urothelial carcinoma of the prostate, non-urothelial and urothelial cancer with variant histology
3. Bone cancer
    i. Ewing's sarcoma
    ii. Mesenchymal chondrosarcoma
    iii. Osteosarcoma
    iv. Dedifferentiated chrondrosarcoma
    v. High-grade undifferentiated pleomorphic sarcoma (UPS)
4. Advanced or recurrent breast cancer.
5. Head and neck cancers (including very advanced head and neck cancer, cancer of the nasopharynx, and salivary gland tumors)
6. Hepatocellular carcinoma

7. Hepatobiliary and biliary tract cancers
    i. Extrahepatic cholangiocarcinoma
    ii. Intrahepatic cholangiocarcinoma
    iii. Gallbladder cancer
8. Hodgkin lymphoma
    i. Classic Hodgkin lymphoma
    ii. Nodular lymphocyte-predominant Hodgkin lymphoma
    iii. Pediatric Hodgkin lymphoma
9. Kidney cancer
10. Malignant pleural or peritoneal mesothelioma
11. Non-small cell lung cancer (NSCLC) other than inoperable locally advanced or metastatic
12. Occult primary tumors (cancer of unknown primary)
13. Persistent, relapsed, or recurrent ovarian cancer,
14. Fallopian tube cancer, and primary peritoneal cancer
15. Malignant germ cell tumors
16. Pancreatic adenocarcinoma
17. Small cell lung cancer (SCLC)
18. Soft tissue sarcoma
    i. Angiosarcoma
    ii. Extremity/Body wall, head/neck
    iii. Retroperitoneal/intra-abdominal
    iv. Rhabdomyosarcoma
    v. Solitary fibrous tumor
    vi. Dermatofibrosarcoma protuberans (DFSP) with fibrosarcomatous transformation
19. Testicular cancer
20. Thymomas and thymic carcinomas
21. Uterine neoplasms (including uterine sarcoma and uterine leiomyosarcoma)
22. Kaposi sarcoma
23. Primary cutaneous lymphomas
    i. Mycosis fungoides/Sezary syndrome
    ii. Primary cutaneous CD30+ T-cell lymphoproliferative disorders
24. T-cell lymphomas
    i. Peripheral T-cell lymphomas
    ii. Adult T-cell leukemia/lymphoma
    iii. Extranodal natural killer (NK)/T-cell lymphoma
    iv. Hepatosplenic T-cell lymphoma
    v. Breast implant-associated anaplastic large cell lymphoma (ALCL)
25. Gestational trophoblastic neoplasia
26. B-Cell lymphomas
    i. Follicular lymphoma (grade 1-2)
    ii. Histologic transformation of indolent lymphoma to diffuse large B-cell lymphoma
    iii. Mantle cell lymphoma
    iv. Diffuse large B-cell lymphoma
    v. High-grade B-cell lymphomas
    vi. Burkitt lymphoma
    vii. HIV-related B-cell lymphomas
    viii. Post-transplant lymphoproliferative disorders
27. Cervical cancer
28. Vulvar cancer
29. Small bowel adenocarcinoma

V. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for all compendial indications other than hepatocellular carcinoma can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

Support for hepatocellular carcinoma can be found in the Micromedex DrugDex database. Use of information in the DrugDex database for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

VI. REFERENCES

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