UnitedHealthcare
Medicare Solutions

Evidence Based Clinical Guidelines

Specialty Drug Criteria

Effective January 1, 2014
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V. Myelodysplastic Syndrome (MDS) (238.72-238.76)
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VIII. Small Cell Lung Cancer (SCLC) (162.0, 162.2-162.5, 162.8, 162.9, 197.0, 198.3, 198.5, V10.11)
IX. Endometrial Cancer (182.0-182.8)
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II. Esophageal and Esophagogastric Junction Cancers (Adenocarcinoma) (150.0-150.5, 150.8, 150.9, 151.0, 235.5)
III. Gastric Cancer (Adenocarcinoma) (151.0-151.6, 151.8, 151.9, 235.2)
J9025  Azacitidine Injection (Vidaza™)

I. **Acute Myelogenous Leukemia (205.00, 205.02)**
   A. Used as a single agent for low-intensity therapy in patients 60 years or older as induction therapy or as post-remission consolidation therapy (3)

II. **Chronic Myeloid Leukemia (205.80, 205.82, 238.72-238.75) (3, 5)**

III. **Myelodysplastic Syndrome (238.72-238.75) (1, 2, 3, 4, 5)**
   A. Treatment of patients with the following myelodysplastic syndrome subtypes:
      1. Refractory anemia or refractory anemia with ringed sideroblasts (if accompanied by neutropenia or thrombocytopenia or requiring transfusion)
      2. Refractory anemia with excess blasts
      3. Refractory anemia with excess blasts in transformation
      4. Chronic myelomonocytic leukemia (CMML)
   B. Initial treatment in lower risk patients with no del (5q) with or without other cytogenetic abnormalities and with
      1. Symptomatic anemia and serum erythropoietin levels greater than 500 mU/mL and a low probability of response to immunosuppressive therapy
      2. Thrombocytopenia or neutropenia
   C. Treatment in lower risk patients with symptomatic anemia with
      1. No del (5q) with or without other cytogenetic abnormalities and no response to initial treatment with erythropoietins or immunosuppressive therapy
      2. Del (5q) with or without other cytogenetic abnormalities and no response to lenalidomide
   D. Preferred treatment in higher risk patients with clinically significant cytopenia(s) who are
      1. Not candidates for high-intensity therapy
      2. High-intensity therapy candidates awaiting improved patient status or donor availability
   E. Treatment in higher risk patients with clinically significant cytopenia(s) who relapse after allogeneic hemopoietic stem cell transplant

References

2. National Comprehensive Cancer Network (NCCN) NCCN Drugs & Biologics Compendium™ Azacitidine; Vidaza®. 07/26/2012
The safety of administering bevacizumab pre or post operatively, in combination with 5FU based regimens has not been adequately evaluated. There should be at least a 6 week interval between the last dose of bevacizumab and elective surgery and at least 6-8 weeks postoperatively. There is an increased risk of stroke and other arterial events especially in age ≥ 65. The use of bevacizumab may interfere with wound healing.

I. Intravitreal therapy for non-oncology indications
   A. Neovascular (wet) age-related macular degeneration (AMD)
   B. Macular edema secondary to:
      1. Diabetes
      2. Branch retinal vein occlusion (BRVO) or
      3. Central retinal vein occlusion (CRVO)
   C. Proliferative diabetic retinopathy
   D. Neovascular glaucoma
   E. Choroidal neovascularization secondary to
      1. Pathologic myopia,
      2. Angioid streaks/pseudoxanthoma elasticum, or
      3. Ocular histoplasmosis syndrome (OHS)
   F. Cystoid macular degeneration (9)
   G. Histoplasmosis retinitis (9)
   H. Neovascular (wet) age-related macular degeneration (9)
   I. Proliferative diabetic retinopathy (9)
   J. Retinal neovascularization (9)
   K. Severe nonproliferative diabetic retinopathy (9)

II. Brain or Central Nervous system cancers
   A. Glioblastoma ¹
   B. Adult intracranial ependymoma (excludes subependymoma and myxopapillary)
      1. As single agent treatment for disease progression after radiation therapy for spine or brain ependymoma recurrence (2A) (2)
   C. Anaplastic gliomas/glioblastomas²
      1. Treatment of recurrent disease or salvage therapy as a single agent or in combination with irinotecan, carmustine, temozolomide for anaplastic Glioma) (2A) (2)
   D. Glioblastoma ²
      1. Treatment of glioblastoma with progressive disease following prior therapy as a single agent or in combination with irinotecan, carmustine, or temozolomide for glioblastoma (FDA, 2A)

III. Breast Cancer
   A. In combination with paclitaxel for patients with recurrent or metastatic or invasive disease that is: (FDA):
1. HER2 Negative
   a. Hormone receptor positive, with visceral crisis (NCCN category 2A)\(^2\)
   b. Either hormone receptor- negative or hormone receptor positive and endocrine therapy refractory (NCCN category 2A)\(^2\)
2. Progressive with no clinical benefit after three consecutive endocrine therapy regimens or with symptomatic visceral disease (NCCN category 2A)\(^2\)

IV. Colorectal Adenocarcinoma
   Avastin is indicated for the first- or second- line treatment of patients with metastatic carcinoma (mCRC) of the colon or rectum in combination with intravenous 5-fluorouracil-based chemotherapy.
   A. Treatment of resectable synchronous liver and or lung metastases (1 & 2)
      1. Neoadjuvant therapy for patients with synchronous liver and/or lung metastases or with resectable metachronous metastases (NCCN compendium category 2A)\(^2\)
      2. Used in combination with one of the following regimes:
         a. FOLFOX (fluorouracil, leucovorin, and oxaliplatin),
         b. FOLFIRI (fluorouracil, leucovorin, and irinotecan), or
         c. CapeOX (capecitabine and oxaliplatin)
   B. Treatment of unresectable synchronous liver and/or lung metastases (NCCN compendium category 2A)\(^2\)
      1. Primary therapy for patients with unresectable synchronous liver and/or lung metastases, with synchronous abdominal/peritoneal metastases, or with unresectable metachronous metastases (NCCN compendium)
   C. Treatment of unresectable advanced or metastatic disease\(^2\)
      1. Initial therapy for patients with unresectable advanced or metastatic disease
         a. For patient who can tolerate intensive therapy in combination with infusional 5-FU/LV in combination with one of the following regimens:
            i. Capecitabine or with
            ii. FOLFOX (fluorouracil, leucovorin, and oxaliplatin),
            iii. FOLFIRI (fluorouracil, leucovorin, and irinotecan),
            iv. 5-FU/LV (fluorouracil and leucovorin), or
            v. CapeOX (capecitabine and oxaliplatin)
         b. For patients who cannot tolerate intensive therapy in combination with
            i. Infusional 5 FU/LV
   D. Used as therapy after first progression of advanced or metastatic disease\(^2\)
      1. In combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin), FOLFIRI
      2. This agent can be used even if it was included in the failed initial regimen.\(^1\)
   E. Not indicated in the adjuvant setting for stage II or III outside of the setting of a clinical trial (NCCN compendium)

V. Non-Small Cell Lung Cancer (NSCLC)
   A. Non-squamous cell histology
      1. First-line treatment (All)
         a. Unresectable, locally advanced, recurrent or metastatic disease (FDA & NCCN category 2A)
         b. Performance status 0-1 (NCCN category 2A)
         c. No history of hemoptysis (NCCN category 2A)
d. In combination with carboplatin and paclitaxel (FDA & NCCN category 2A)
2. Single agent continuation maintenance therapy (NCCN category 2A)
   a. First-line with chemotherapy (All)
      i. Recurrence or metastasis with tumor response or stable disease following first-line chemotherapy
      ii. Performance status 0-1
      iii. No history of hemoptysis
B. Adenocarcinoma (NCCN category 2A)
   1. Second-line therapy (All)
      a. If erlotinib was given first-line
      b. Performance status 0-2
      c. In combination with a platinum based doublet

VI. Ovarian Cancer
A. Epithelial Ovarian Cancer/ Fallopian Tube Cancer/Primary Peritoneal Cancer (NCCN category 2A)
   1. Single Agent: (Any)
      a. Progressive, stable, or persistent disease on primary chemotherapy
      b. Relapse after complete remission following primary chemotherapy
      c. Stage II-IV disease showing partial response to primary treatment
B. Ovarian stromal tumors (NCCN category 2A) (All)
   1. Granulosa cell histology
   2. Clinical relapse in patients with stage II-IV disease

VII. Sarcoma
A. Soft tissue sarcoma- angiosarcoma
   1. Used as a single agent (NCCN category 2A)
B. Solitary fibrous tumor
   1. In combination with temozolomide (NCCN category 2A)
C. Hemangiopericytoma
   1. In combination with temozolomide (NCCN Category 2A)

VIII. Renal Cell Carcinoma (1, 2)
A. Metastatic carcinoma, in combination with interferon alfa (NCCN category 1)
B. Metastatic carcinoma, after progression on prior cytokine therapy (NCCN category 2A)

IX. Malignant Neoplasm of Connective Tissue (171.0—171.9) (3)
References:

1. Avastin (bevacizumab) FDA Prescribing Information. Accessed 1/31/2013
2. NCCN Drugs and Biologics Compendium, Bevacizumab. Accessed 7/31/2012
7. L31836 Local Coverage Determination (LCD) for Chemotherapy and Biologicals, CGS Administrators, (15202) Ohio, Accessed 8/01/2012
9. L29959 Local Coverage Determination (LCD) for Bevacizumab (AVASTIN®); First Coast Service Options (MAC Part B) (09102) Florida. Accessed 8/01/2012
I. Multiple Myeloma- Systemic Light Chain Amyloidosis (277.30)
   A. Primary treatment as a single agent or in combination with dexamethasone
      1. For combination with dexamethasone and cyclophosphamide or lenalidomide and
         (NCCN 1,2A)
      2. For combination with dexamethasone in nontransplant candidates (NCCN 1,2A)
   B. Preferred maintenance therapy as a single agent for
      1. Active (symptomatic) myeloma responding to primary myeloma therapy (NCCN 2A)
      2. Stable or responsive disease following stem cell transplant (NCCN 2A)

II. Non-Hodgkin’s Lymphoma
   A. Mantle cell lymphoma (200.40-200.48, V10.79)
      1. Second-line therapy with or without rituximab for relapsed, refractory, or progressive
disease
      1. Second-line therapy for patients with
         a. Stage IA-IIA MF with histologic evidence of folliculotropic or large cell transformation or
            stage IIB with generalized extent tumor, transformed, and/or folliculotropic disease in
            combination with skin-directed therapy
         b. Stage IV non-Sezary or visceral disease
         c. Refractory or progressive stage III MF or SS
      2. Single agent therapy for tumors with histologic evidence of large cell transformation and
         aggressive growth rate in non-candidates for transplant with:
         a. Stage IA-IIA MF with histologic evidence of folliculotropic or large cell transformation or
            stage IIB with generalized extent tumor, transformed, and/or folliculotropic disease in
            combination with skin directed therapy
         b. Stage IV non-Sezary or visceral disease
      1. Second-line therapy for relapsed or refractory angioimmunoblastic T-cell lymphoma,
        peripheral T-cell lymphoma not otherwise specified, anaplastic large cell lymphoma, or
        enteropathy-associated T-cell lymphoma in non-candidates for transplant

III. Solitary Plasmacytoma; Smoldering Multiple Myeloma; Multiple Myeloma
      (203.00, 203.10, 203.80, 238.6, V10.79)
   A. Primary chemotherapy for progressive solitary plasmacytoma or smoldering myeloma
      (asymptomatic) that has progressed to active (symptomatic) myeloma in
      1. Combination with dexamethasone with or without cyclophosphamide, doxorubicin,
         lenalidomide or thalidomide for transplant candidates (all preferred regimens)
      2. Combination with dexamethasone or in MPB (melphalan, prednisone, and bortezomib)
         regimen for non-transplant candidates (all preferred regimens)
   B. Preferred maintenance therapy as a single agent for
      1. Active (symptomatic) myeloma responding to primary myeloma therapy
2. Stable or responsive disease following stem cell transplant

C. Salvage therapy on or off clinical trials for disease relapse after 6 months following primary chemotherapy with the same regimen in
   1. Combination with dexamethasone with or without cyclophosphamide, doxorubicin, lenalidomide, or thalidomide for transplant candidates
   2. Combination with dexamethasone or in MPB (melphalan, prednisone, and bortezomib) regimen for non-transplant candidates

D. Salvage therapy on or off clinical trials for disease relapse or for progressive or refractory disease
   1. As a single agent
   2. In combination with dexamethasone with or without lenalidomide or cyclophosphamide
   3. In combination with liposomal doxorubicin
   4. In VTD-PACE (bortezomib, dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide, and etoposide) regimen

IV. Waldenström's Macroglobulinemia/ Lymphoplasmacytic Lymphoma (200.80-200.88, 273.3, V10.79)
   A. Used as a single agent or in combination with rituximab with or without dexamethasone as
      1. Primary therapy
      2. Salvage therapy for disease that does not respond to primary therapy or for progressive or relapsed disease

V. Anaplastic Large Cell Lymphoma (200.60-200.68)

VI. Peripheral T-cell Lymphoma (202.70-202.78)

VII. Other Lymphomas (202.80-202.88)

VIII. Amyloidosis (277.30)

References:

Retrospective subset analyses of metastatic or advanced colorectal cancer trials have not shown a treatment benefit for cetuximab in patients whose tumors had KRAS mutations in codon 12 or 13. Use of cetuximab is not recommended for the treatment of colorectal cancer with these mutations. Consult the full FDA label with particular attention to boxed warning(s).

I. Colon Cancer (Adenocarcinoma)
   A. Tumors expressing KRAS wild-type gene
      1. Used in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen as
         a. Neoadjuvant therapy for patients with synchronous liver and/or lung metastases or with resectable metachronous metastases
         b. Adjuvant therapy for patients with metachronous metastases
         c. Primary therapy for patients with unresectable synchronous liver and/or lung metastases, with synchronous abdominal/peritoneal metastases, or with unresectable metachronous metastases
   B. Tumors expressing KRAS wild-type gene with unresectable advanced or metastatic disease
      1. As single agent or in combination with irinotecan after first progression except in patients receiving capecitabine or fluorouracil and leucovorin with bevacizumab
      2. In combination with FOLFIRI (fluorouracil, leucovorin, and irinotecan) after first progression in patients who previously received FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) regimen with or without bevacizumab
      3. As a single agent or in combination with irinotecan after second or third progression except in patients receiving cetuximab or panitumumab for first progression

II. Head and Neck Cancers (Squamous Cell Carcinoma with Mixed Subtypes)
   A. Advanced, recurrent, persistent
      1. Primary concurrent chemoradiation as a single agent for
         a. Newly diagnosed T4b, any N or unresectable nodal disease with no metastases in performance status (PS) 2 patients
         b. Unresectable locoregional recurrence in PS 2 patients who have not received prior radiation therapy (RT)
         c. Resectable locoregional recurrence in patients who have not received prior RT
      2. Therapy
         a. As a single agent
            i. For patients with performance status (PS) 3
               01. With newly diagnosed T4b
               02. Any N or unresectable nodal disease with no metastases or with unresectable locoregional recurrence and
               03. No prior radiation therapy (RT)
            ii. For patients with performance status (PS) 0-2
b. In combination with carboplatin and fluorouracil or cisplatin with or without fluorouracil for
   i. Patients with performance status (PS) 0-1 with unresectable locoregional recurrence or
   ii. As second primary in patients who have received prior RT or for distant metastases

B. Cancer of the glottic larynx
   1. Primary concurrent chemoradiation as a single agent
      a. For T3, N0-3 disease requiring total laryngectomy
      b. Consider for selected T4a patients who decline surgery
   2. Primary concurrent chemoradiation as a single agent for
      a. T1, N+
      b. Selected T2, N0, or T2-3, any N disease requiring total laryngectomy
   3. Sequential chemoradiation
      a. For T4a, any N disease with partial response at the primary site and at least stable disease in the neck following induction chemotherapy
      b. T4a, any N disease with complete response at the primary site to induction chemotherapy

C. Cancer of the lip
   1. Primary concurrent chemoradiation as a single agent for patients with
      a. T3-4a, N0 or
      b. Any T, N1-3 disease who are poor surgical risks

D. Cancer of the oropharynx
   1. Primary concurrent chemoradiation as a single agent for
      a. T1, N1 disease
      b. T3-4a, N0-1 disease
      c. Any T, N2-3 disease

E. Cancer of the supraglottic larynx
   1. Primary concurrent chemoradiation as a single agent for
      a. T3, N0 and most T3, N2-3 disease requiring laryngectomy
      b. T1-2, N+ and selected T3, N1 disease not requiring total laryngectomy
      c. Consider for T4a, N0-3 patients who decline surgery

F. Ethmoid sinus tumors
   1. Primary concurrent chemoradiation as a single agent for
      a. Newly diagnosed T3-4b disease
      b. Patients who decline surgery
      c. Cancer diagnosed after incomplete excision with gross residual disease

G. Maxillary sinus tumors
   1. Primary concurrent chemoradiation as a single agent for T4b, any N

III. Non-small Cell Lung Cancer (NSCLC) (Adenocarcinoma (with Mixed Subtypes); Squamous Cell Carcinoma; Large Cell Carcinoma)
   A. Single agent continuation maintenance therapy if given first-line with chemotherapy for recurrence or metastasis in patients with performance status 0-2 who achieve tumor response or stable disease following first-line chemotherapy
IV. Rectal Cancer (Adenocarcinoma)
   A. Tumors expressing KRAS wild-type gene with unresectable advanced or metastatic disease
      1. Initial therapy in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin)
      2. As a single agent or in combination with irinotecan after first progression (except in patients receiving capecitabine or fluorouracil and leucovorin with bevacizumab)
      3. As a single agent or in combination with irinotecan after second or third progression (except in patients receiving cetuximab or panitumumab for first progression)

V. Pancreatic Cancer (157.0-157.9)§

References

2. L29097 Local Coverage Determination (LCD) for Cetuximab (Erbitux®) First Coast Service Options, Inc. (09102) Florida Accessed 08/01/2012.
8. C. J. Punt, J. Tol, C. J. Rodenburg, et al. Randomized phase III study of capecitabine, oxaliplatin, and bevacizumab with or without cetuximab in advanced colorectal cancer (ACC), the CAIRO2 study of the Dutch Colorectal Cancer Group (DCCG) J Clinical Oncology, 2008: LBA4011 Available at: http://meeting.ascopubs.org/cgi/content/abstract/26/15_suppl/LBA4011
10. A48896 (10102) Local Coverage Article for Drugs and Biologicals - Chemotherapeutic Agents, Cahaba Government Benefit Administrators Alabama Accessed 8/1/2012
I. Bone Metastases from Solid Tumors

A. Denosumab (Xgeva) is indicated for the treatment of bone metastases in patients with solid tumors. (ICD-9 198.5 plus ICD-9 of original cancer) (1,2,3,4,5)
B. Denosumab is not indicated for treatment of patients with Multiple Myeloma. (203.0, 238.6) (1,2,3,5)
C. Hypocalcemia must be corrected before treatment. (1,2,3,5)

References

1. Local Coverage Article for Denosumab (Prolia™, Xgeva™) (A50745) (MAC-Part B) (KY, ID, OH); CGS Administrators, LLC.
2. Local Coverage Article for Denosumab (Prolia™, Xgeva™)- related to LCD L25820 (A50745) (MAC-Part B) (NY, CT); National Government Services, Inc.
3. Local Coverage Determination (LCD) for Chemotherapy and Biologicals (L31836) (MAC-Part B) (KY, ID, OH). CGS Administrators, LLC.
4. L25820- Drugs and Biologicals, Coverage of, for Label and Off-Label Uses (MAC-Part B) (NY, CT). National Government Services, Inc.
5. Prescribing Information Xgeva (Denosumab) Injection, for subcutaneous use.
Q2050  Doxorubicin Hydrochloride, 10 mg (Doxil®)

I.  Breast Cancer- Invasive (174.0-174.6, 174.8, 175.0, 175.9, V10.3)
   A.  Preferred single agent for patients with recurrent or metastatic disease that is
       1.  (HER2)- (human epidermal growth factor receptor 2) negative visceral crisis
       2.  HER-2-positive, previously treated with Herceptin (trastuzumab) or trastuzumab planned
           or contraindicated, and either hormone receptor-negative or hormone receptor-positive
           and endocrine therapy refractory or with visceral crisis
       3.  HER2- negative and either hormone receptor-negative or hormone receptor-positive and
           endocrine therapy refractory

II. Hodgkin's Lymphoma
   A.  Classical Hodgkin’s lymphoma (201.50-201.58, 201.60-201.68, 201.70-201.78, 201.90-201.98,
       V10.72)
       1.  Second-line treatment as a component of GVD (gemcitabine, vinorelbine, and liposomal
           doxorubicin) regimen with or without radiation therapy (RT) prior to autologous stem cell
           rescue for progressive disease or for relapsed disease in patients initially treated with
           chemotherapy alone or in combination with RT
   B.  Lymphocyte-predominant Hodgkin's lymphoma (201.40-201.48, V10.72)
       1.  Second-line treatment as a component of GVD (gemcitabine, vinorelbine, and liposomal
           doxorubicin) regimen with or without radiation therapy (RT) prior to autologous stem cell
           rescue for progressive disease or for relapsed disease in patients initially treated with
           chemotherapy alone or in combination with RT

III. Non-Hodgkin's Lymphoma
   A.  NHL-AIDS-related B-cell lymphoma (042 with 200.70-200.78, 202.80-202.88)
       1.  In combination with growth factor support (and rituximab if CD20+) for AIDS related diffuse
           large B-cell lymphoma, primary effusion lymphoma, and lymphoma associated with
           Castleman's disease as a component of CDOP (cyclophosphamide, liposomal
           doxorubicin, vincristine, and prednisone) regimen
       1.  First-line chemotherapy for patients with
           a.  Stage IA-IIIA MF with histologic evidence of folliculotropic or large cell transformation or
               stage IIB with generalized extent tumor, transformed, and/or folliculotropic disease in
               combination with skin-directed therapy
           b.  Stage IV non-Sezary or visceral disease
           c.  Refractory or progressive stage III MF or SS
   C.  NHL-All N HL subtypes if there is pre-existing left ventricular dysfunction or dysfuntion develops
       while on treatment or patient has received 550 mg/m² of Doxorubicin (4)

IV. Ovarian Cancer- Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary
    Peritoneal Cancer (158.8, 183.0, 183.2-183.5, 183.8, 183.9, V10.43)
   A.  Preferred single-agent recurrence therapy, if platinum resistant, for
1. Progressive, stable, or persistent disease on primary chemotherapy
2. Relapse after complete remission following primary chemotherapy
3. Stage II-IV disease showing partial response to primary treatment

B. Preferred recurrence chemotherapy, if platinum-sensitive, in combination with carboplatin for
   1. Progressive, stable, or persistent disease on primary chemotherapy
   2. Relapse after complete remission for 6 or more months following primary chemotherapy
   3. Stage II-IV disease showing partial response to primary treatment

V. Soft Tissue Sarcoma- Retroperitoneal/Intra-abdominal (158.0, 158.8, 158.9, 171.5, 171.9)
   A. Soft tissue sarcoma- retroperitoneal/intra-abdominal (158.0, 158.8, 158.9, 171.5, 171.9)
      1. Single agent for
         a. Preoperative chemotherapy for resectable disease at initial presentation or for recurrent disease
         b. Unresectable or metastatic disease at initial presentation or for progressive or recurrent disease
         c. Angiosarcoma
   B. Soft tissue sarcoma of the extremity/trunk (171.0, 171.2, 171.3, 171.7, 171.9)
      1. Single agent for
         a. Primary treatment as chemotherapy or chemoradiation for unresectable primary disease
         b. Adjuvant chemotherapy or chemoradiation for unresectable primary disease that becomes resectable following preoperative treatment
         c. Palliative chemotherapy for unresectable disease following primary treatment
         d. Primary treatment alone, or before or after metastasectomy with or without radiation therapy for single-organ confined, limited tumor bulk stage IV or recurrent disease that is amenable to complete resection
         e. Palliative chemotherapy for stage IV or recurrent disease with disseminated metastases
         f. Angiosarcoma

VI. Solitary Plasmacytoma; Smoldering Multiple Myeloma; Multiple Myeloma (203.00, 203.10, 203.80, 238.6)
   A. Salvage therapy on or off clinical trials in combination with bortezomib for disease relapse or for progressive or refractory disease

VII. Uterine Neoplasms- Endometrial Carcinoma (182.0)
    A. Uterine Neoplasms- Endometrial Carcinoma (182.0)
       1. Primary treatment as a single agent
          a. With sequential radiation therapy (RT), surgery, and brachytherapy for extrauterine pelvic disease
          b. Consider following palliative hysterectomy with bilateral salpingo-oophorectomy, RT, and hormonal therapy for extra-abdominal or liver disease
       2. For completely surgically staged patients as a single agent
          a. With sequential pelvic radiation therapy (RT) and/or vaginal brachytherapy in patients with stage IB disease with histologic grade 3 tumors and adverse risk factors
b. With sequential pelvic RT and vaginal brachytherapy in patients with stage II disease with histologic grade 3 tumors

c. With or without sequential tumor-directed RT for stage IIA, IIB, and IIIC disease

d. With or without sequential RT for stage IV disease

3. Single agent

a. For asymptomatic or low-grade disseminated metastases that have progressed on hormonal therapy

b. With or without sequential palliative radiation therapy (RT) for symptomatic, grade 2-3, or large volume metastases

c. With sequential tumor-directed RT with or without brachytherapy for local recurrence in patients with disease confined to the vagina or in pelvic, para-aortic, or common iliac lymph nodes

d. With or without sequential tumor-directed RT for microscopic upper abdominal or peritoneal recurrences

e. Local recurrence in patients who have received prior external-beam RT to site of recurrence

B. Uterine Neoplasms- endometrial carcinoma (papillary serous or clear cell carcinoma) (182.0)

1. Single agent with or without sequential tumor-directed radiation therapy following hysterectomy with bilateral salpingo-oophorectomy

References


2. L28576, Chemotherapy Drugs and their Adjuncts, MAC- Part B: Wisconsin Physicians Service Insurance Corporation (05202), Iowa, Kansas, Missouri, Nebraska: Accessed 08/02/2012.


I. **Bladder Cancer (Transitional Cell Carcinoma; Squamous Cell Carcinoma; Adenocarcinoma)**
   A. **Neoadjuvant chemotherapy in combination with cisplatin**
      1. Strongly consider for patients with node-negative clinical stage T3 disease who receive radical cystectomy
      2. Can be considered for patients with node-negative clinical stage T2 disease who receive radical or segmental cystectomy
   B. **Primary treatment in combination with cisplatin**
      1. For patients with node-negative clinical stage T2-3 disease with extensive comorbid disease or poor performance status
      2. With or without sequential radiation therapy for clinical stage T4 and node-positive T3 disease
   C. **Chemotherapy in combination with cisplatin**
      1. For metastatic disease
      2. With or without sequential radiation therapy for local recurrence following cystectomy
      3. For patients with muscle-invasive disease with local recurrence following bladder-sparing treatment who are not eligible for surgery
   D. May be considered as second-line therapy as a single agent for metastatic disease

II. **Bladder Cancer- Upper GU Tract Tumors (Transitional Cell Carcinoma; Squamous Cell Carcinoma; Adenocarcinoma)**
   A. **Neoadjuvant therapy in selected patients with operable renal pelvic tumors that are large, high grade, or with parenchymal invasion**
   B. **Neoadjuvant therapy in selected patients with urothelial carcinoma of the upper, mid (high-grade tumors only), and distal ureter**
   C. **Metastatic disease**
   D. **Adjuvant chemotherapy in combination with cisplatin with or without sequential radiation therapy for pathologic stage T2-4 or nodal disease (pN+) of the renal pelvis and transitional cell carcinoma of the ureter**
   E. **May be considered as second-line therapy as a single agent for metastatic disease**

III. **Bladder Cancer- Urothelial Carcinoma of the Prostate (Transitional Cell Carcinoma)**
   A. **Chemotherapy in combination with cisplatin following cystoprostatectomy with or without urethrectomy for stromal invasion for**
      1. Neoadjuvant or adjuvant disease
      2. Advanced or metastatic disease

IV. **Bone Cancer**
A. Ewing’s sarcoma
   1. Used in combination with docetaxel with or without vincristine and growth factor support for
      a. Relapse with or without radiation therapy
      b. Progressive disease following primary treatment
B. Osteosarcoma (8) (NCCN 2A)
   1. Second-line therapy as a single agent or in combination with docetaxel

V. Breast Cancer
A. Breast Cancer- Invasive
   1. Preferred single agent or as a preferred combination with paclitaxel for patients with
      recurrent or metastatic disease that is
      a. Hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-
         negative with visceral crisis
      b. HER2-negative and either hormone receptor-negative or hormone receptor-positive
         and endocrine therapy refractory
      c. Progressive with no clinical benefit after three consecutive endocrine therapy regimens
         or with symptomatic visceral disease

VI. Head & Neck Cancer (Squamous Cell Carcinoma with Mixed Subtypes) (8) (NCCN 2A)
A. Single agent for patients with cancer of the nasopharynx with performance status 0-2 with:
   1. Newly diagnosed T4b, any N or unresectable nodal disease with no metastases in patients
      with performance status (PS) 2
   2. Unresectable locoregional recurrence in patients with PS 2 who have not received prior
      radiation therapy (RT)
   3. Unresectable locoregional recurrence or second primary in patients with PS 0-2 who have
      received prior RT
   4. Distant metastases in patients with performance status (PS) 0-2

VII. Hepatobiliary Cancers- Extrahepatic Cholangiocarcinoma (Adenocarcinoma)
A. Hepatobiliary Cancers- Extrahepatic cholangiocarcinoma (Adenocarcinoma)
   1. As a single agent or in combination with capecitabine, oxaliplatin, or cisplatin as:
      a. Primary treatment for unresectable or metastatic disease
      b. Secondary or adjuvant treatment in patients with resected disease with positive
         regional lymph nodes
   2. Secondary or adjuvant treatment as a single agent
      a. Following fluoropyrimidine chemoradiation (brachytherapy or external beam) in
         patients with resected disease with positive margins (R1) or gross residual disease
         (R2), carcinoma in situ at margin, or positive regional nodes
      b. In patients with resected disease with negative margins (R0) and negative regional
         nodes
B. Hepatobiliary Cancers- Gallbladder cancer
   1. Primary treatment in patients with unresectable or metastatic disease
      a. As a single agent
      b. In combination with capecitabine, cisplatin, or oxaliplatin
   2. Adjuvant treatment as a single agent in patients with resected disease other than T1b, N0
C. Hepatobiliary Cancers- intrahepatic cholangiocarcinoma
1. As a single agent or in combination with capecitabine, oxaliplatin, or cisplatin as
   a. Primary treatment for unresectable or metastatic disease
   b. Adjuvant treatment for resected disease with microscopic surgical margins (R1 resection) or residual local disease (R2 resection)

VIII. Hodgkin’s Lymphoma - Classical Hodgkin’s Lymphoma
   A. Second-line treatment (with or without radiation therapy (RT)) for relapsed disease in patients initially treated with chemotherapy alone or in combination with RT as a component of
      1. GVD (gemcitabine, vinorelbine, and liposomal doxorubicin) regimen
      2. IGEV (ifosfamide, gemcitabine, and vinorelbine) regimen
      3. GCD (gemcitabine, carboplatin, and dexamethasone) regimen

IX. Malignant Pleural Mesothelioma
   A. First-line treatment in combination with cisplatin as
      1. Adjuvant treatment for clinical stage II-III disease
      2. Treatment of unresectable or medically inoperable clinical stage I-III disease
      3. Treatment of clinical stage IV disease or tumors of sarcomatoid histology
   B. Second-line treatment as a single agent

X. Non-Hodgkin’s Lymphoma
   A. AIDS-related B-cell lymphoma
      1. Second-line therapy with or without rituximab for relapse of AIDS-related diffuse large B-cell lymphoma, primary effusion lymphoma, and lymphoma associated with Castleman’s disease as a component of
         a. GDP (gemcitabine, dexamethasone, and cisplatin) regimen
         b. GemOx (gemcitabine and oxaliplatin) regimen
   B. Burkitt Lymphoma
      1. Second-line therapy for relapse of Burkitt lymphoma following complete response as a component of RGDP (rituximab, gemcitabine, dexamethasone, and cisplatin) regimen
   C. Diffuse large B-cell lymphoma
      1. Second-line therapy with or without rituximab for relapsed or refractory disease as a component of
         a. GDP (gemcitabine, dexamethasone, and cisplatin) regimen
         b. GemOx (gemcitabine and oxaliplatin) regimen
   D. Follicular lymphoma and Nodal marginal zone lymphoma
      1. Second-line therapy with or without rituximab for refractory or progressive disease as a component of
         a. GDP (gemcitabine, dexamethasone, and cisplatin) regimen
         b. GemOx (gemcitabine and oxaliplatin) regimen
         c. Gastric MALT lymphoma
      2. Second-line therapy with or without rituximab for recurrent or progressive disease in patients with the indications for treatment as a component of
         a. GDP (gemcitabine, dexamethasone, and cisplatin) regimen
         b. GemOx (gemcitabine and oxaliplatin) regimen
   E. Mantle cell lymphoma
1. Second-line therapy with or without rituximab for relapsed, refractory, or progressive disease as a component of
   a. GDP (gemcitabine, dexamethasone, and cisplatin) regimen
   b. GemOx (gemcitabine and oxaliplatin) regimen

F. Mycosis fungoides (MF)/Sezary Syndrome (SS)
   1. First-line chemotherapy for patients with
      a. Stage IA-IIA Mycosis fungoides with histologic evidence of folliculotropic or large cell transformation or stage IIB with generalized extent tumor, transformed, and/or folliculotropic disease in combination with skin-directed therapy
      b. Stage IV non-Sezary or visceral disease
      c. Refractory or progressive stage III MF or SS
   2. Chemotherapy for tumors with histologic evidence of large cell transformation and aggressive growth rate as a component of
      a. GDP (gemcitabine, dexamethasone, and cisplatin) or GemOx (gemcitabine and oxaliplatin) regimen in candidates for transplant or
      b. As a single agent in non-candidates for transplant with stage IA-IIA MF with histologic evidence of folliculotropic or large cell transformation or stage IIB with generalized extent tumor, transformed, and/or folliculotropic disease in combination with skin directed therapy
      c. Stage IV non-Sezary or visceral disease

G. Nongastric MALT lymphoma
   1. Second-line therapy with or without rituximab for recurrent stage I-II disease or for progressive disease in patients with the indications for treatment as a component of
      a. GDP (gemcitabine, dexamethasone, and cisplatin) regimen
      b. GemOx (gemcitabine and oxaliplatin) regimen

H. Peripheral T-cell Lymphoma
   1. Second-line therapy for relapsed or refractory angioimmunoblastic T-cell lymphoma, peripheral T-cell lymphoma not otherwise specified, anaplastic large cell lymphoma, or enteropathy-associated T-cell lymphoma
   2. In candidates for transplant as a component of
      a. GDP (gemcitabine, dexamethasone, and cisplatin) regimen or
      b. GemOx (gemcitabine and oxaliplatin) regimen
      c. As a single agent in non-candidates for transplant

I. Primary cutaneous B-cell lymphoma
   1. Second-line therapy for primary cutaneous marginal zone or follicle center B-cell lymphoma with or without rituximab for refractory generalized cutaneous disease or relapsed generalized extracutaneous disease as a component of
      a. GDP (gemcitabine, dexamethasone, and cisplatin) regimen
      b. GemOx (gemcitabine and oxaliplatin) regimen
   2. Second-line therapy with or without rituximab for relapsed or refractory primary cutaneous diffuse large B-cell lymphoma, leg type as a component of
      a. GDP (gemcitabine, dexamethasone, and cisplatin) regimen
      b. GemOx (gemcitabine and oxaliplatin) regimen

J. Splenic marginal zone lymphoma
   1. Second-line therapy for primary cutaneous marginal zone or follicle center B-cell lymphoma with or without rituximab for refractory generalized cutaneous disease or relapsed generalized extracutaneous disease as a component of
a. GDP (gemcitabine, dexamethasone, and cisplatin) regimen
b. GemOx (gemcitabine and oxaliplatin) regimen
2. Second-line therapy with or without rituximab for relapsed or refractory primary cutaneous diffuse large B-cell lymphoma, leg type as a component of
   a. GDP (gemcitabine, dexamethasone, and cisplatin) regimen
   b. GemOx (gemcitabine and oxaliplatin) regimen

XI. Non-small Cell Lung Cancer
A. Adjuvant chemotherapy in combination with cisplatin for \(^8\) (NCCN 1;2A)
B. Stage 1B and above First-line therapy for recurrence or metastasis
   1. In combination with cisplatin, carboplatin or docetaxel in performance status (PS) 0-2 or elderly patients
   2. As a single agent in PS 2 or elderly patients
   3. Second line treatment in patients who have not had previous progression on a regimen including this drug \(^8\) (NCCN 2A)
C. First-line therapy in cisplatin- or carboplatin- based regimens in combination with bevacizumab for recurrence or metastasis in patients with performance status 0-1
D. Neoadjuvant for T3-4, N0-1\(^8\) (NCCN 2A)

XII. Occult Primary
A. Chemoradiation in combination with cisplatin or docetaxel in symptomatic patients with performance status (PS) 1-2 or asymptomatic patients with PS 0 and aggressive disease for localized disease with inguinal nodal involvement
B. In combination with cisplatin or docetaxel in symptomatic patients with performance status (PS) 1-2 or asymptomatic patients with PS 0 and aggressive disease for
   1. Lung disease or hormone receptor-negative pleural effusion
   2. Resectable liver disease
   3. Peritoneal mass with non-ovarian histology unresectable liver disease or disseminated metastases
   4. Unresectable liver disease or disseminated metastases \(^8\) (NCCN 2A)

XIII. Ovarian Cancer- Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer
A. Evidence of resistance or progression must include clinical findings in addition to unchanged or rising CA 125 (Treatment based on CA 125 alone are NCCN 2B)
B. Preferred single-agent recurrence therapy, if platinum resistant for
   1. Progressive, stable, or persistent disease on primary chemotherapy
   2. Relapse after complete remission following primary chemotherapy
   3. Stage II-IV disease showing partial response to primary treatment
C. Preferred recurrence chemotherapy, if platinum sensitive, in combination with cisplatin or carboplatin for
   1. Progressive, stable or persistent disease on primary chemotherapy
   2. Relapse after complete remission for 6 or more months following primary chemotherapy
   3. Stage II-IV disease showing partial response to primary treatment
XIV. **Pancreatic Cancer (Adenocarcinoma)**
   A. Induction chemotherapy as therapy for unresectable or locally advanced disease
   B. Adjuvant treatment
      1. As systemic chemotherapy before and after fluoropyrimidine- or gemcitabine-base concurrent chemoradiation
      2. As a single agent
   C. Single-agent therapy for patients with locally advanced unresectable or metastatic disease (Category 1; 2A) for patients with locally advanced disease and good performance status
   D. For patients with locally advanced or metastatic disease and good performance status
      1. In combination with one of the following
         a. Capecitabine
         b. Or erlotinib
   E. Second-line therapy as a single agent for patients with progressive disease and good performance status who have received prior fluoropyrimidine-based therapy

XV. **Small Cell Lung Cancer (SCLC)**
   A. Subsequent chemotherapy as a single agent for
      1. Relapse within 6 months following complete or partial response with initial treatment
      2. Primary progressive disease (performance status 0-2)

XVI. **Soft Tissue Sarcoma**
   A. Retroperitoneal/Intra-abdominal
      1. Single agent or in combination with docetaxel or vinorelbine for
         a. Unresectable or metastatic disease at initial presentation or for progressive or recurrent disease
         b. Angiosarcoma

XVII. **Soft Tissue Sarcoma of the Extremity/Trunk**
   A. Single agent or in combination with docetaxel or vinorelbine for
      1. Adjuvant chemotherapy or chemoradiation for resectable stage II-III disease (primary tumors or local recurrence)
      2. Primary treatment as chemotherapy or chemoradiation for unresectable primary disease
      3. Adjuvant chemotherapy or chemoradiation for unresectable primary disease that becomes resectable following preoperative treatment
      4. Palliative chemotherapy for unresectable disease following primary treatment
      5. Primary treatment alone, or before or after metastasectomy with or without radiation therapy for single-organ confined, limited tumor bulk stage IV or recurrent disease that is amenable to complete resection
      6. Palliative chemotherapy for stage IV or recurrent disease with disseminated metastases
      7. Angiosarcoma

XVIII. **Testicular Cancer (Nonseminoma; Pure Seminoma)**
   A. As palliative chemotherapy in combination with oxaliplatin after second-line or high-dose chemotherapy regimens

XIX. **Thymomas and Thymic Carcinomas**
A. Second-line therapy as a single agent following radiation therapy for locally advanced unresectable disease

XX. **Uterine Cancer- Uterine Sarcoma (Undifferentiated Sarcoma, Leiomyosarcoma)**
   A. Single agent or in combination with docetaxel
      1. For unresectable disease limited to the uterus
      2. Following TH/BSO for stage IV disease
      3. For local recurrence confined to the vagina in patients who have received prior radiation therapy (RT)
      4. For extrapelvic recurrence with no prior RT
      5. For isolated metastases consider postoperative chemotherapy for resectable isolated metastases
      6. Or disseminated metastases

XXI. **Cancer of the pineal gland (194.4)***

XXII. **Letterer-Siwe disease/ Histiocytosis-X (202.50-202.58)***

XXIII. **Germ Cell Tumors and Ovarian Germ Cell Tumors***

References

7. A46103 (Related to LCD L25820) Local Coverage Article for Gemcitabine Hydrochloride (e.g., Gemzar®) – () National Government Services, Inc. MAC Par B Connecticut Accessed 8/8/2012.
J9228 Iplimumab (Yervoy™)

I. Melanoma (172.0-172.9, 190.9, 198.3, 199.0, 199.1, V10.82)
   A. Single agent for
      1. Unresectable stage III in-transit metastases
      2. Local/satellite and/or in-transit unresectable recurrence
      3. Incompletely resected nodal recurrence
      4. Limited recurrence or metastatic disease
      5. Disseminated recurrence or metastatic disease (2) (NCCN 1)

References

I. Autoimmune Diseases
   A. Autoimmune Mucocutaneous Blistering Disease/ Pemphigus and Pemphigoid (NCD-FDA off label)
      1. Used as a short term therapy for:
         a. Pemphigus vulgaris
         b. Pemphigus foliaceus
         c. Bullous pemphigoid
         d. Mucous membrane pemphigoid
         e. Cicatrical pemphigoid
         f. Epidermolysis bullosa
      2. AND one of the following criteria:
         a. Failure on a previous conventional therapy
         b. Contraindication of previous therapy
         c. Rapidly progressing disease
   B. Autoimmune diabetes mellitus
   C. Autoimmune uveitis
   D. Fetomaternal alloimmune thrombocytopenia
   E. Graves ophthalmopathy
   F. Idiopathic thrombocytopenic purpura (ITP)
   G. Inflammatory myopathies (Dermatomyositis, Polymyositis)
   H. Posttransfusion purpura
   I. Severe rheumatoid arthritis

II. Infectious and Infection Related Disease
    A. Bacterial infections in lymphoproliferative disease
    B. Cytomegalovirus (CMV) induced pneumonitis in solid organ transplants
    C. Enteroviral meningoencephalitis
    D. Kawasaki disease
    E. Neonatal sepsis
    F. Rotaviral enterocolitis
    G. Staphylococcal toxic shock

III. Other Miscellaneous Uses
A. Chronic inflammatory demyelinating polyneuropathy
B. Guillain-Barre’ syndrome (GBS)
C. IgM antmyelin-associated glycoprotein paraprotein-associated peripheral neuropathy
D. Lambert-Eaton myasthenic syndrome
E. Monoclonal gammopathy
F. Relapsing-remitting multiple sclerosis
G. Multifocal motor neuropathy (MMN)
H. Myasthenia gravis
I. Rasmussen syndrome
J. Stiff-man syndrome

IV. Primary and Secondary Immune Deficiencies
   A. Chronic lymphocytic leukemia (CLL)
   B. Pediatric human immunodeficiency virus (HIV)
   C. High-risk, preterm, low birth weight neonatal infections
   D. Primary humoral immunodeficiency (FDA label)
   E. Wiskot-Aldrich Syndrome (4)
   F. Common Variable Immunodeficiency Syndrome (4)

V. Pre or Post Transplant of the following
   A. For kidney transplant AND one of the following:
      1. Prophylaxis to reduce transplant rejection before transplant
      2. Prophylaxis to reduce transplant rejection after transplant
      3. Treatment of acute rejection

VI. Bone Marrow Transplantation

VII. Chronic Parvovirus B19 Infection with Severe Anemia Secondary to Bone Marrow Suppression

VIII. Erythema Multiforme

IX. Hyperimmunoglobulinemia E. Syndrome

X. Multifocal Motor Neuropathy

XI. Multiple Myeloma

XII. Other Specified Bullous Dermatoses
References:

1. UHC IVIG drug policy # 2010D0035D
J9264  Paclitaxel Protein-Bound Particles for Injectable Suspension; 1 MG (Abraxane®)

I.  Breast Cancer- Invasive (174.0-174.6, 174.8, 174.9, 175.0, 175.9, V10.3)
   A.  Preferred single agent for patients with recurrent or metastatic disease that is presenting as visceral crisis (NCCN 2A)
   B.  ER/PR positive and HER 2 negative or positive and no response to three consecutive endocrine therapy regimens [NCCN breast cancer monograph recommends trastuzumab + chemotherapy, which could include a taxane (NCCN 2A)
   C.  ER/PR negative and HER2 negative (NCCN 2A)

II. Non-small Cell Lung Cancer (NSCLC) (Adenocarcinoma (with mixed subtypes); Squamous Cell Carcinoma; Large Cell Carcinoma) (162.0, 162.2-162.5, 162.8, 162.9, V10.11)
    A.  Locally advanced or metastatic Non-Small Cell Lung Cancer (NSCLC), as first-line treatment in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy. (5)

III. Ovarian Cancer- Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer (158.8, 183.0, 183.2-183.5, 183.8, 183.9, V10.43)
    A.  Recurrence therapy as a single agent if evidence for recurrence is a finding other than CA125. For (Treatment based on CA 125 alone are NCCN 2B)
       1.  Progressive, stable, or persistent disease on primary chemotherapy
       2.  Relapse after complete remission following primary chemotherapy if relapse is less than 6 months after platinum therapy (NCCN 2A)
       3.  Stage II-IV disease showing partial response to primary treatment

IV.  Anal Cancer

V.  Occult Primary
    A.  Symptomatic patients with ECOG PS 0-2
    B.  Asymptomatic patients with histologically aggressive tumors
References


2. L28576, Chemotherapy Drugs and their Adjuncts, MAC- Part B: Wisconsin Physicians Service Insurance Corporation (05202), Iowa, Kansas, Missouri, Nebraska.: Accessed 08/08/2012.


I. **Colorectal Cancer (Adenocarcinoma)**
   A. Tumors expressing KRAS wild-type gene
      1. Used in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen
      2. Neoadjuvant therapy for patients with synchronous liver and/or lung metastases or with resectable metachronous metastases
      3. Primary therapy for patients with unresectable synchronous liver and/or lung metastases, with synchronous abdominal/peritoneal metastases, or with unresectable metachronous metastases
   B. Tumors expressing KRAS wild-type gene with unresectable advanced or metastatic disease
      1. Initial therapy in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin)
      2. Initial therapy in combination with FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen as therapy
         a. After first progression following FOLFOX (fluorouracil, leucovorin, oxaliplatin, and irinotecan)
         b. After first progression following CapeOX (capecitabine and oxaliplatin) regimen with or without bevacizumab for patients who can tolerate intensive therapy
   C. Tumors expressing KRAS wild-type gene who have unresectable advanced or metastatic disease and are not able to tolerate cetuximab plus irinotecan
      1. As a single agent after first progression following FOLFIRI (fluorouracil, leucovorin, and irinotecan) with or without bevacizumab or FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen
      2. After second or third progression except in patients receiving cetuximab or panitumumab for first progression

II. **Penile cancer** *(NCCN 2A)*
   A. Second line treatment for unresectable or metastatic disease expressing KRAS wild type
References:


I. Cervical Cancer\(^7\) (NCCN 3, but listed in FL LCD)
   A. Previously untreated cervical cancer

II. Nonsquamous Non-Small Cell Lung Cancer (NSCLC) (Adenocarcinoma (with mixed subtypes); Large Cell Carcinoma)
   A. Adjuvant chemotherapy in combination with cisplatin for
      1. Stage IB, IIA, and IIB (T3, N0; T2b, N1)
      2. Resectable or marginally resectable superior sulcus tumors (T3 invasion, T4 extension, N0-1)
      3. T3 invasion or T4 extension, N0-1 tumors in the chest wall, proximal airway, or mediastinum if not given as initial treatment
      4. T1-2, T3 7 or more cm, N2, M0 with stable disease or local progression
      5. Margin-negative separate pulmonary nodule(s)
   B. First-line therapy for recurrence or metastasis for tumors of nonsquamous cell histology
      1. In combination with cisplatin or carboplatin in patients with performance status (PS) 0-2 or elderly patients
      2. In cisplatin- or carboplatin- based regimens in combination with bevacizumab in patients with PS 01, tumors of nonsquamous cell histology, and no history of hemoptysis
      3. As a single agent in PS 2 or elderly patients
   C. Single-agent for recurrence or metastasis in patients with performance status 0-2 with tumors of nonsquamous cell histology who achieve tumor response or stable disease following first-line chemotherapy as switch maintenance
   D. Second-line therapy as a single agent for progressive disease in patients with performance status 0-2 with tumors of nonsquamous cell histology
   E. Neoadjuvant treatment for T3 or T4 tumor or extension in the chest wall, proximal airway, or medianistinum \(^3\) (NCCN 2A)

III. Malignant Pleural Mesothelioma (Epithelial, Sarcomatoid)
   A. Induction therapy in combination with cisplatin for medically operable clinical stage II-III disease
   A. May be considered as second-line therapy as a single agent for metastatic disease
   B. Induction therapy in combination with cisplatin for medically operable clinical stage II-III disease
   C. Used in combination with cisplatin or carboplatin as
      1. Adjuvant treatment for clinical stage II-III disease
      2. First-line treatment of unresectable or medically inoperable clinical stage I-III disease
      3. First-line treatment of clinical stage IV disease or tumors of sarcomatoid histology
      4. Second-line treatment if not administered first line
IV. Bladder Cancer- Upper GU Tract Tumors (Transitional Cell Carcinoma; Squamous Cell Carcinoma; Adenocarcinoma)
   A. May be considered as second-line therapy as a single agent for metastatic disease

V. Ovarian Cancer- Epithelial Ovarian Cancer/Fallopian Tube Cancer/ Primary Peritoneal Cancer
   A. Single-agent recurrence therapy, if platinum resistant, for
      1. Progressive, stable, or persistent disease on primary chemotherapy treatment
      2. Relapse after complete remission following primary chemotherapy treatment
      3. Stage II-IV disease showing partial response to primary treatment

VI. Thymomas and Thymic Carcinomas
   A. Second-line therapy as a single agent following radiation therapy for locally advanced unresectable disease

VII. Malignant neoplasm of pleura (11)

References:

7. L29255 Local Coverage Determination (LCD) for Pemetrexed First Coast Service Options, Inc.(09102 MAC-Part B) (FL). Accessed 8/13/2012
9. Retired
10. L28576 Local Coverage Determination (LCD) for Chemotherapy Drugs and their Adjuncts –Wisconsin Physicians Service Insurance Corporation (05102, 05302, 05402) - MAC - Part B) Iowa, Missouri, Nebraska Accessed 8/13/2012
J9310  Rituximab (Rituxan®)

(All Leptomeningeal metastases are covered in indications below – “A” is a compendium note only – not listed in the monograph. Details by indication are listed below)

I. Hodgkin’s Lymphoma- Lymphocyte- Predominant Hodgkin’s Lymphoma
   A. Primary treatment with or without radiation therapy for patients with stage IB or IIB or stage III-IV disease as a single agent or as a component of one of the following regimens
      1. ABVD (doxorubicin, bleomycin, vinblastine, and dacarbazine)
      2. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone)
      3. CVP (cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone)
      4. EPOCH (cyclophosphamide, doxorubicin, etoposide, vincristine, and prednisone)

II. Immune or Idiopathic Thrombocytopenia Purpura
   A. For the treatment of refractory thrombotic thrombocytopenic purpura (TTP) for patients who do not respond to plasmapheresis

III. Non Hodgkin’s Lymphoma
   A. AIDS-related B-cell lymphoma
      1. In combination with growth factor support as a component of one of the following regimens
         a. CODOX-M (cyclophosphamide, doxorubicin, and vincristine with intrathecal methotrexate and cytarabine followed by high-dose systemic methotrexate) regimen alternating with IVAC (ifosfamide, cytarabine, etoposide, and intrathecal methotrexate) with rituximab
         b. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) regimen with rituximab for favorable presentation
         c. CDE (cyclophosphamide, doxorubicin, and etoposide) with rituximab for favorable presentation
         d. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) with high-dose methotrexate and with rituximab for favorable presentation
      2. In combination with growth factor support for CD20+ AIDS related diffuse large B-cell lymphoma and lymphoma associated with Castleman’s disease
         a. As a component of one of the following regimens
            i. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) with rituximab
            ii. CDE (cyclophosphamide, doxorubicin, and etoposide) with rituximab
            iii. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) with rituximab
            iv. CDOP (cyclophosphamide, liposomal doxorubicin, vincristine, and prednisone) with rituximab
         a. As a component of one of the following regimens in patients with intention to proceed to high-dose therapy with autologous stem cell rescue
i. DHAP (dexamethasone, cisplatin, and cytarabine)
ii. ESHAP (etoposide, methylprednisolone, cytarabine, and cisplatin)
iii. GDP (gemcitabine, dexamethasone, and cisplatin)
iv. GemOX (gemcitabine and oxaliplatin)
v. ICE (ifosfamide, carboplatin, and etoposide)
vi. MINE (mesna, ifosfamide, mitoxantrone, and etoposide)

b. As a single agent

c. In combination with lenalidomide

d. As a component of one of the following regimens in patients who are not candidates for high-dose therapy
   i. CEPP (cyclophosphamide, etoposide, prednisone, and procarbazine)
   ii. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin)
   iii. CEOP (cyclophosphamide, etoposide, vincristine, and prednisone)
   iv. GDP
   v. GemOx regimen with rituximab

B. Burkitt's lymphoma

1. Induction therapy for low-risk disease as a component of one of the following regimens
   a. CODOX-M (cyclophosphamide, doxorubicin, and vincristine, with intrathecal methotrexate and cytarabine followed by high-dose systemic methotrexate) (original or modified) with rituximab
   b. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) with rituximab and intrathecal methotrexate
   c. HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with high-dose methotrexate and cytarabine with rituximab

2. Induction therapy for high-risk disease as a component of one of the following regimens
   a. CODOX-M (cyclophosphamide, doxorubicin, and vincristine, with intrathecal methotrexate) with rituximab
   b. HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with high-dose methotrexate and cytarabine with rituximab
   c. Second-line therapy for relapse of Burkitt's lymphoma following complete response as a component of one of the following regimens:
      i. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) with rituximab and intrathecal methotrexate
      ii. RGDP (rituximab, gemcitabine, dexamethasone, and cisplatin)
      iii. For patients not able to tolerate aggressive therapy- dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) with rituximab and intrathecal methotrexate
      iv. If not previously given- RIVAC (rituximab, ifosfamide, cytarabine, etoposide, and intrathecal methotrexate)

C. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic lymphoma

1. First-line therapy for stage II-IV disease
   a. In combination with alemtuzumab, bendamustine, or high-dose methylprednisolone for CLL with del(17p)
   b. In combination with bendamustine for CLL without del(17p) or with or without del(11q)
   c. In combination with fludarabine for CLL without del(11q) or with or without del(17p)
   d. In patients age 70 years or older or younger patients with comorbidities
i. As single-agent therapy in patients unable to tolerate purine analogs or for CLL without del(17p) or with or without del(11q)
ii. In combination with cyclophosphamide and prednisone for CLL without del(17p) or with or without del(11q)
iii. As a component of PCR (pentostatin, cyclophosphamide, and rituximab) regimen for CLL without del(17p) or with or without del(11q)
iv. As a component of reduced-dose FCR for CLL with del(11q)
e. In patients less than age 70 years or in older patients without significant comorbidities or for CLL with del(17p)
i. As a component of FCR (fludarabine, cyclophosphamide, and rituximab) regimen for CLL without del(17p) or with or without del(11q)

2. Therapy for relapsed or refractory CLL
a. Without del(11q) or del(17p) as a single agent, in combination with bendamustine, or as a component of cyclophosphamide and prednisone with rituximab, FCR (fludarabine, cyclophosphamide, and rituximab), FR (fludarabine and rituximab) or PCR (pentostatin, cyclophosphamide, and rituximab) regimen for patients with a long response (more than 3 years) to first-line therapy
b. With del(11q) as a single agent, in combination with bendamustine, or as a component of cyclophosphamide and prednisone with rituximab, FCR, reduced-dose FCR, or PCR regimen
c. Without del(17p) or with or without del(11q) in combination with bendamustine, alemtuzumab, or high-dose methylprednisolone or as a component of FCR, PCR, CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) with rituximab, HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with high-dose methotrexate and cytarabine with rituximab, dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) with rituximab, or OFAR (oxaliplatin, fludarabine, cytarabine, and rituximab) regimen in patients less than age 70 years or in older patients without significant comorbidities with a short response (less than 2 years) to first-line therapy

3. Therapy for relapsed or refractory CLL with del(17p) in combination with alemtuzumab, bendamustine, or high-dose dexamethasone or as a component of
a. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) with rituximab regimen
b. HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with high-dose methotrexate and cytarabine with rituximab regimen
c. OFAR (oxaliplatin, fludarabine, cytarabine, and rituximab) regimen
d. CFAR (cyclophosphamide, fludarabine, alemtuzumab, and rituximab) regimen

D. Diffuse large B-cell lymphoma
1. First-line therapy for stage I-II disease as a component of CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen with rituximab
2. First-line therapy for stage III to IV disease as a component of
   a. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen with rituximab
   b. Dose-dense CHOP 14 regimen with rituximab
3. First-line therapy in patients with poor left ventricular function as a component of
   a. CEPP (cyclophosphamide, etoposide, prednisone, and procarbazine) regimen with rituximab
b. CDOP (cyclophosphamide, liposomal doxorubicin, vincristine, and prednisone) regimen with rituximab

c. CNOP (cyclophosphamide, mitoxantrone, vincristine, and prednisone) regimen with rituximab

d. Dose-adjusted EPOCH regimen with rituximab

e. CEOP (cyclophosphamide, etoposide, vincristine, and prednisone) regimen with rituximab

4. Second-line therapy for relapsed or refractory disease

a. As a component of one of the following regimens with rituximab in patients with intention to proceed to high-dose therapy with autologous stem cell rescue

i. DHAP (dexamethasone, cisplatin, and cytarabine)

ii. ESHAP (etoposide, methylprednisolone, cytarabine, and cisplatin)

iii. GDP (gemcitabine, dexamethasone, and cisplatin)

iv. GemOX (gemcitabine and oxaliplatin)

v. ICE (ifosfamide, carboplatin and etoposide)

vi. MINE (mesna, ifosfamide, mitoxantrone, and etoposide)

b. As a single agent

c. In combination with lenalidomide

d. Or as a component of one of the following regimens with rituximab in non-candidates for high-dose therapy

i. CEPP (cyclophosphamide, etoposide, prednisone, and procarbazine)

ii. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin)

iii. CEOP (cyclophosphamide, etoposide, vincristine and prednisone)

iv. GDP

v. GemOX

E. Follicular lymphoma and nodal marginal zone lymphoma

1. First-line therapy

a. As a single agent or

b. In combination with chlorambucil or cyclophosphamide in elderly or infirm patients with the indications for treatment in the setting of comorbidities where tolerability of combination chemotherapy is a concern

2. First-line therapy

a. As a single agent or

b. In combination with one of the following regimens

i. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen with rituximab

ii. CVP (cyclophosphamide, vincristine, and prednisone) regimen with rituximab

iii. Fludarabine with rituximab

iv. FND (fludarabine, mitoxantrone, and dexamethasone) regimen with rituximab

v. Bendamustine with rituximab

vi. CHOP regimen with rituximab followed by radioimmunotherapy

vii. CVP regimen with rituximab followed by radioimmunotherapy

viii. Fludarabine with rituximab followed by radioimmunotherapy

ix. FND regimen with rituximab followed by radioimmunotherapy

3. Second-line therapy for refractory or progressive disease in patients

a. With the indications for treatment as a single agent
b. Or in combination with one of the following regimens
   i. Bendamustine with rituximab
   ii. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen with rituximab
   iii. CVP (cyclophosphamide, vincristine, and prednisone) regimen with rituximab
   iv. Fludarabine with rituximab
   v. FND (fludarabine, mitoxantrone, and dexamethasone) regimen with rituximab
   vi. FCMR (fludarabine, cyclophosphamide, mitoxantrone, and rituximab) regimen
   vii. DHAP (dexamethasone, cisplatin, and cytarabine) regimen with rituximab
   viii. ESHAP (etoposide, methylprednisolone, cytarabine, and cisplatin) regimen with rituximab
   ix. GDP (gemcitabine, dexamethasone, and cisplatin) regimen with rituximab
   x. GemOX (gemcitabine and oxaliplatin) regimen with rituximab
   xi. ICE (ifosfamide, carboplatin, and etoposide) regimen with rituximab
   xii. MINE (mesna, ifosfamide, mitoxantrone, and etoposide) regimen with rituximab
   xiii. CEPP (cyclophosphamide, etoposide, prednisone, and procarbazine) regimen with rituximab
   xiv. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) regimen with rituximab
   xv. CEOP (cyclophosphamide, etoposide, vincristine, and prednisone) regimen with rituximab
   xvi. Lenalidomide with rituximab

4. Maintenance therapy as first-line (up to two years) or second-line extended dosing

F. Gastric MALT lymphoma
   1. Initial therapy as a single agent for patients with H. pylori-negative stage I<sub>E</sub>-II<sub>E</sub> disease if radiation is contraindicated
   2. First-line therapy
      a. As a single agent or
      b. In combination with chlorambucil or cyclophosphamide for stage III<sub>E</sub>-IV disease in elderly or infirm patients with the indications for treatment in the setting of comorbidities where tolerability of combination chemotherapy is a concern
   3. First-line therapy for stage III<sub>E</sub>-IV disease
      a. As a single agent
      b. In combination with one of the following regimens
         i. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen with rituximab
         ii. CVP (cyclophosphamide, vincristine, and prednisone) regimen with rituximab
         iii. Fludarabine with rituximab
         iv. FND (fludarabine, mitoxantrone, and dexamethasone) regimen with rituximab
         v. Bendamustine with rituximab
         vi. CHOP regimen with rituximab followed by radioimmunotherapy
         vii. CVP regimen with rituximab followed by radioimmunotherapy
         viii. Fludarabine with rituximab followed by radioimmunotherapy
         ix. FND regimen with rituximab followed by radioimmunotherapy
   4. Second-line therapy for recurrent or progressive disease
      a. In patients with the indications for treatment as a single agent or in
         i. Bendamustine with rituximab
ii. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen with rituximab
iii. CVP (cyclophosphamide, vincristine, and prednisone) regimen with rituximab
iv. Fludarabine with rituximab
v. FND (fludarabine, mitoxantrone, and dexamethasone) regimen with rituximab
vi. FCMR (fludarabine, cyclophosphamide, mitoxantrone, and rituximab) regimen
vii. DHAP (dexamethasone, cisplatin, and cytarabine) regimen with rituximab
viii. ESHAP (etoposide, methylprednisolone, cytarabine, and cisplatin) regimen with rituximab
ix. GDP (gemcitabine, dexamethasone, and cisplatin) regimen with rituximab
x. GemOX (gemcitabine and oxaliplatin) regimen with rituximab
xi. ICE (ifosfamide, carboplatin, and etoposide) regimen with rituximab
xii. MINE (mesna, ifosfamide, mitoxantrone, and etoposide) regimen with rituximab
xiii. CEPP (cyclophosphamide, etoposide, prednisone, and procarbazine) regimen with rituximab
xiv. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) regimen with rituximab
xv. CEOP (cyclophosphamide, etoposide, vincristine, and prednisone) regimen with rituximab
xvi. Lenalidomide with rituximab

5. Maintenance therapy as first-line (up to two years) or second-line extended dosing

G. Lymphoblastic lymphoma

1. Induction or reinduction therapy for stage I-IV disease as a component of HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine) regimen with rituximab in CD20-positive disease and with imatinib in Philadelphia chromosome-positive disease

H. Mantle cell lymphoma

1. Induction therapy as a component of aggressive therapy with
   a. HyperCVAD (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with high-dose methotrexate and cytarabine regimen with rituximab
   b. NORDIC (dose-intensified induction immunochemotherapy with rituximab, cyclophosphamide, vincristine, doxorubicin, and prednisone [maxi-CHOP] alternating with rituximab and high-dose cytarabine) regimen
   c. Rituximab + methotrexate with augmented CHOP (CALGB regimen)
   d. Sequential RCHOP/RICE (rituximab, ifosfamide, carboplatin, and etoposide)
   e. Sequential RCHOP/RDHAP (rituximab, dexamethasone, cisplatin, and cytarabine) regimen followed by cytarabine

2. Induction therapy as a component of less aggressive therapy with
   a. Bendamustine or cladribine
   b. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen with rituximab
   c. CVP (cyclophosphamide, vincristine, and prednisone) with rituximab
   d. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) regimen with rituximab
e. Modified Hyper CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) regimen with rituximab followed by rituximab maintenance in patients older than 65 years

3. Second-line therapy for relapsed, refractory or progressive disease
   a. In combination with
      i. Bendamustine
      ii. Bortezomib
      iii. Cladribine
      iv. Lenalidomide
   b. Or as a component of one of the following regimens
      i. FC (fludarabine and cyclophosphamide) regimen with rituximab
      ii. PEPC (prednisone, etoposide, procarbazine, and cyclophosphamide) regimen with rituximab
      iii. PCR (pentostatin, cyclophosphamide, and rituximab) regimen
      iv. FMR (fludarabine, mitoxantrone, and rituximab) regimen
      v. FCMR (fludarabine, cyclophosphamide, mitoxantrone, and rituximab) regimen
      vi. DHAP (dexamethasone, cisplatin, and cytarabine) regimen with rituximab
      vii. ESHAP (etoposide, methylprednisolone, cytarabine, and cisplatin) regimen with rituximab
      viii. GDP (gemcitabine, dexamethasone, and cisplatin) regimen with rituximab
      ix. GemOX (gemcitabine and oxaliplatin) regimen with rituximab
     x. ICE (ifosfamide, carboplatin, and etoposide) regimen with rituximab
     xi. MINE (mesna, ifosfamide, mitoxantrone, and etoposide) regimen with rituximab
     xii. CEPP (cyclophosphamide, etoposide, prednisone, and procarbazine) regimen with rituximab
     xiii. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) regimen with rituximab
     xiv. CEOP (cyclophosphamide, etoposide, vincristine, and prednisone) regimen with rituximab

I. Nongastric MALT lymphoma
   1. First-line therapy
      a. As a single agent or
      b. In combination with chlorambucil or cyclophosphamide for stage III-IV disease in elderly or infirm patients with the indications for treatment in the setting of comorbidities where tolerability of combination chemotherapy is a concern
   2. First-line therapy for MALT lymphomas coexistent with large cell lymphoma as a component of one of the following regimens:
      a. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) with rituximab for stage I-II disease
      b. CHOP with rituximab
      c. Dose-dense CHOP 14 with rituximab
      d. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) with rituximab for stage III-IV disease
   3. First-line therapy for MALT lymphomas coexistent with large cell lymphoma in patients with poor left ventricular function as a component of one of the following regimens
      a. CEPP (cyclophosphamide, etoposide, prednisone, and procarbazine) with rituximab
b. CDOP (cyclophosphamide, liposomal doxorubicin, vincristine, and prednisone) with rituximab
c. CNOP (cyclophosphamide, mitoxantrone, vincristine, and prednisone) with rituximab
d. Dose-adjusted EPOCH with rituximab
e. CEOP (cyclophosphamide, etoposide, vincristine, and prednisone) with rituximab

4. First-line therapy for stage III-IV disease
a. As a single agent
b. In combination with one of the following regimens
   i. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen with rituximab
   ii. CVP (cyclophosphamide, vincristine, and prednisone) regimen with rituximab
   iii. Fludarabine with rituximab
   iv. FND (fludarabine, mitoxantrone, and dexamethasone) regimen with rituximab
   v. Bendamustine with rituximab
   vi. CHOP regimen with rituximab followed by radioimmunotherapy
   vii. CVP regimen with rituximab followed by radioimmunotherapy
   viii. Fludarabine with rituximab followed by radioimmunotherapy
   ix. FND regimen with rituximab followed by radioimmunotherapy

5. Second-line therapy for recurrent stage I-II disease or for progressive disease
a. In patients with the indications for treatment as a single agent or
b. In combination with one of the following regimens
   i. Bendamustine with rituximab
   ii. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen with rituximab
   iii. CVP (cyclophosphamide, vincristine, and prednisone) regimen with rituximab
   iv. Fludarabine with rituximab
   v. FND (fludarabine, mitoxantrone, and dexamethasone) regimen with rituximab
   vi. FCMR (fludarabine, cyclophosphamide, mitoxantrone, and rituximab) regimen
   vii. DHAP (dexamethasone, cisplatin, and cytarabine) regimen with rituximab
   viii. ESHAP (etoposide, methylprednisolone, cytarabine, and cisplatin) regimen with rituximab
   ix. GDP (gemcitabine, dexamethasone, and cisplatin) regimen with rituximab
   x. GemOX (gemcitabine and oxaliplatin) regimen with rituximab
   xi. ICE (ifosfamide, carboplatin, and etoposide) regimen with rituximab
   xii. MINE (mesna, ifosfamide, mitoxantrone, and etoposide) regimen with rituximab
   xiii. CEPP (cyclophosphamide, etoposide, prednisone, and procarbazine) regimen with rituximab
   xiv. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) regimen with rituximab
   xv. CEOP (cyclophosphamide, etoposide, vincristine, and prednisone) regimen with rituximab
   xvi. Lenalidomide with rituximab

6. Maintenance therapy as first-line (up to two years) or second-line extended dosing

J. Post transplant lymphoproliferative disorder (PTLD)
   1. Single-agent therapy as
      a. Primary treatment for monomorphic or polymorphic PTLD
b. Second-line treatment for persistent or progressive early lesions or for persistent or progressive monomorphic PTLD if reduction of immunosuppressive was used as initial therapy
c. Maintenance therapy for polymorphic PTLD achieving complete response on primary treatment

2. Primary treatment of monomorphic or systemic polymorphic PTLD or second-line treatment of persistent or progressive monomorphic or polymorphic PTLD when used as a component of one of the following regimens
   a. RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen
   b. RCHOEP (rituximab, cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone) regimen
   c. RCVP (rituximab, cyclophosphamide, vincristine, and prednisone) regimen (for patients who cannot tolerate anthracyclines)

K. Primary central nervous system lymphoma
   1. Primary systemic treatment combined with high-dose methotrexate, vincristine, procarbazine, and cytarabine and with or without radiation therapy
   2. Treatment as a single agent or in combination with temozolomide for progressive disease in patients who have received prior methotrexate-based regimen without prior radiation therapy
      a. After prolonged response to prior regimen
      b. In combination with radiation therapy after short or no response to prior regimen
   3. Consider systemic and/or intracerebrospinal fluid treatment as a single agent or in combination with temozolomide for progressive or recurrent disease in patients with prior whole brain radiation therapy

L. Primary cutaneous B-cell lymphoma
   1. Therapy for generalized T3 cutaneous primary cutaneous marginal zone or follicle center B-cell lymphoma
      a. As a single agent
      b. As palliative chemotherapy in combination with CVP (cyclophosphamide, vincristine, and prednisone) regimen or chlorambucil
   2. Therapy for primary cutaneous marginal zone or follicle center B-cell generalized T3 cutaneous disease or newly diagnosed generalized extracutaneous disease in elderly or infirm patients with indications for treatment in the setting of comorbidities and the ability to tolerate combination chemotherapy is a concern
      a. Used as a single agent (preferred)
      b. In combination with chlorambucil
      c. In combination with cyclophosphamide
   3. Therapy for primary cutaneous marginal zone or follicle center B-cell refractory generalized cutaneous disease or newly diagnosed or relapsed generalized extracutaneous disease
      a. As a single agent
      b. In combination with Bendamustine with rituximab
      c. In combination with one of the following regimens
         i. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen with rituximab
         ii. CVP (cyclophosphamide, vincristine, and prednisone) regimen with rituximab
         iii. Fludarabine with rituximab
iv. FND (fludarabine, mitoxantrone, and dexamethasone) regimen with rituximab  

v. CHOP regimen with rituximab followed by radioimmunotherapy  

vi. CVP regimen with rituximab followed by radioimmunotherapy  

vii. Fludarabine with rituximab followed by radioimmunotherapy  

viii. FND regimen with rituximab followed by radioimmunotherapy  

4. Second-line therapy for primary cutaneous marginal zone or follicle center B-cell refractory  
   generalized cutaneous disease or relapsed generalized extracutaneous disease in patients  
   with the indications for treatment  
   a. As a single agent or  
   b. In Bendamustine with rituximab  
   c. In combination with one of the following regimens  
      i. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen with  
         rituximab  
      ii. CVP (cyclophosphamide, vincristine, and prednisone) regimen with rituximab  
      iii. Fludarabine with rituximab  
      iv. FND (fludarabine, mitoxantrone, and dexamethasone) regimen with rituximab  
      v. FCMR (fludarabine, cyclophosphamide, mitoxantrone, and rituximab) regimen  
      vi. DHAP (dexamethasone, cisplatin, and cytarabine) regimen with rituximab  
      vii. ESHAP (etoposide, methylprednisolone, cytarabine, and cisplatin) regimen with  
         rituximab  
      viii. GDP (gemcitabine, dexamethasone, and cisplatin) regimen with rituximab  
      ix. GemOX (gemcitabine and oxaliplatin) regimen with rituximab  
      x. ICE (ifosfamide, carboplatin, and etoposide) regimen with rituximab  
      xi. MINE (mesna, ifosfamide, mitoxantrone, and etoposide) regimen with rituximab  
      xii. CEPP (cyclophosphamide, etoposide, prednisone, and procarbazine) regimen with  
         rituximab  
      xiii. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide,  
            and doxorubicin) regimen with rituximab  
      xiv. CEOP (cyclophosphamide, etoposide, vincristine, and prednisone) regimen with  
         rituximab  
      xv. Lenalidomide with rituximab  

5. First-line therapy for generalized cutaneous T3 primary cutaneous diffuse large B-cell  
   lymphoma, leg type as a component of CHOP (cyclophosphamide, doxorubicin, vincristine,  
   and prednisone) regimen with rituximab  

6. First-line therapy for solitary regional, T1-2 or extracutaneous primary cutaneous diffuse  
   large B-cell lymphoma, leg type as a component of one of the following regimens:  
   a. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen with  
      rituximab  
   b. Dose-dense CHOP 14 regimen with rituximab  
   c. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and  
      doxorubicin) regimen with rituximab  

7. First-line therapy in patients with poor left ventricular function as a component of  
   a. CEPP (cyclophosphamide, etoposide, prednisone, and procarbazine) regimen with  
      rituximab  
   b. CDOP (cyclophosphamide, liposomal doxorubicin, vincristine, and prednisone)  
      regimen with rituximab
c. CNOP (cyclophosphamide, mitoxantrone, vincristine, and prednisone) regimen with rituximab

d. Dose-adjusted EPOCH regimen with rituximab

e. CEOP (cyclophosphamide, etoposide, vincristine, and prednisone) regimen with rituximab

8. Second-line therapy for relapsed or refractory primary cutaneous diffuse large B-cell lymphoma, leg type

a. In patients where the intent is to proceed to high-dose therapy with autologous stem cell rescue
   i. As a component of one of the following regimens
      01. DHAP (dexamethasone, cisplatin, and cytarabine)
      02. ESHAP (etoposide, methylprednisolone, cytarabine, and cisplatin)
      03. GDP (gemcitabine, dexamethasone, and cisplatin)
      04. GemOX (gemcitabine and oxaliplatin)
      05. ICE (ifosfamide, carboplatin, and etoposide)
      06. MINE (mesna, ifosfamide, mitoxantrone, and etoposide)

b. In patients who are not candidates for high-dose therapy
   i. As a single agent
   ii. In combination with Lenalidomide
   iii. As a component of one of the following regimens
       01. CEPP (cyclophosphamide, etoposide, prednisone, and procarbazine)
       02. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin)
       03. CEOP (cyclophosphamide, etoposide, vincristine, and prednisone)
       04. GDP
       05. GemOX regimen with rituximab in non-candidates for high-dose therapy

M. Splenic marginal zone lymphoma

1. In patients with symptomatic hepatitis C-negative with splenomegaly
   a. Single-agent therapy

2. In elderly or infirm patients with disease progression following initial treatment for splenomegaly where tolerability of combination chemotherapy is a concern due to comorbidities as first-line therapy
   a. As a single agent or
   b. In combination with chlorambucil or cyclophosphamide

3. For progressive disease following initial treatment for splenomegaly as first-line therapy
   a. As a single agent or
   b. In combination with one of the following regimens
      i. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen with rituximab
      ii. CVP (cyclophosphamide, vincristine, and prednisone) regimen with rituximab
      iii. Fludarabine with rituximab
      iv. FND (fludarabine, mitoxantrone, and dexamethasone) regimen with rituximab
      v. Bendamustine with rituximab
      vi. CHOP regimen with rituximab followed by radioimmunotherapy
      vii. CVP regimen with rituximab followed by radioimmunotherapy
      viii. Fludarabine with rituximab followed by radioimmunotherapy
      ix. FND regimen with rituximab followed by radioimmunotherapy
4. For recurrent or progressive disease in patients with the indications for treatment as second-line therapy
   a. As single agent or
   b. In with one of the following regimens
      i. Bendamustine with rituximab
      ii. CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen with rituximab
      iii. CVP (cyclophosphamide, vincristine, and prednisone) regimen with rituximab
      iv. Fludarabine with rituximab
      v. FND (fludarabine, mitoxantrone, and dexamethasone) regimen with rituximab
      vi. FCMR (fludarabine, cyclophosphamide, mitoxantrone, and rituximab) regimen
      vii. DHAP (dexamethasone, cisplatin, and cytarabine) regimen with rituximab
      viii. ESHAP (etoposide, methylprednisolone, cytarabine, and cisplatin) regimen with rituximab
      ix. GDP (gemcitabine, dexamethasone, and cisplatin) regimen with rituximab
      x. GemOX (gemcitabine and oxaliplatin) regimen with rituximab
      xi. ICE (ifosfamide, carboplatin, and etoposide) regimen with rituximab
      xii. MINE (mesna, ifosfamide, mitoxantrone, and etoposide) regimen with rituximab
      xiii. CEPP (cyclophosphamide, etoposide, prednisone, and procarbazine) regimen with rituximab
      xiv. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) regimen with rituximab
      xv. CEOP (cyclophosphamide, etoposide, vincristine, and prednisone) regimen with rituximab
      xvi. Lanalidomide with rituximab

5. Maintenance therapy as first-line (up to two years) or second-line extended dosing

N. Waldenström’s Macroglobulinemia/Lymphoplasmacytic lymphoma
   1. Used as primary therapy, as salvage therapy for disease that does not respond to primary therapy, or for progressive or relapsed disease
      a. As a single agent
      b. In combination with bortezomib with or without dexamethasone
      c. In combination with thalidomide
      d. In combination with cyclophosphamide and prednisone or dexamethasone
      e. In combination with bendamustine (risk of stem cell toxicity and/or transformation unknown)
   2. Used in combination with cladribine or fludarabine in non-transplant candidates as
      a. Primary therapy
      b. Salvage therapy for disease that does not respond to primary therapy or for progressive or relapsed disease
   3. Consider for maintenance therapy in patients who achieve a complete or partial response to primary therapy

IV. Microscopic Polyangiitis (MPA)
   A. Rituximab in combination with glucocorticoids is indicated for the treatment of adult patients

V. Rheumatoid Arthritis (RA)
A. Rituximab in combination with methotrexate to reduce signs and symptoms and to slow the progression of structural damage in adult patients with moderately-to severely-active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies.

VI. Wegener’s Granulomatosis (WG)
A. Rituximab in combination with glucocorticoids is indicated for the treatment of adult patients

VII. Alpha-1-antitrypsin deficiency (273.4) (11)

VIII. Autoimmune hemolytic anemias (283.0) (11)

IX. Primary thrombocytopenia, unspecified - congenital and hereditary thrombocytopenic purpura (287.30 - 287.33) (11)

X. Polyarteritis nodosa (446.0) (11)

XI. Wegener's granulomatosis (446.4) (11)

XII. Thrombotic microangiopathy (446.6) (11)

XIII. Pemphigus - benign mucous membrane pemphigoid with ocular involvement (694.4 - 694.61) (11)

XIV. Acquired coagulation factor deficiency (286.7) (9)

XV. Acquired hemophilia (286.52) (9)

XVI. Multicentric Castleman's disease associated with human herpesvirus infection in HIV-infected patients (785.6) (9)

XVII. Microscopic polyangiitis (MPA) (Effective-FDA (446.0) (9)

XVIII. Acute refractory and relapsed refractory thrombotic thrombocytopenic purpura (TTP) due to immune-mediated ADAMTS-13 deficiency. (446.6) (9)

XIX. Polymyositis (710.4) (9)

XX. Multiple Sclerosis (340) (12)

XXI. Graft versus Host disease unspecified (279.50) (12)

XXII. Other Human Herpes Virus Infection (058.89) (12)

XXIII. Complications of Transplants (12)
A. Kidney (998.81)
B. Heart (996.83)
C. Bone Marrow (996.85)

XXIV. Enlargement of Lymphnodes (785.6)\(^{(12)}\)

References

6. L29271 Local Coverage Determination (LCD) for Rituximab (Rituxan®) First Coast Service Options, Inc. (09102- MAC- Part B) Florida Accessed 08/13/2012
8. Retired
11. A48896 Local Coverage Article for Drugs and Biologicals - Chemotherapeutic Agents; Cahaba Government Benefit Administrators (10102, 10202, 10302) Alabama, Georgia, Tennessee. 08/13/2012
12. A49636 Related to LCD L25820 Local Coverage Article for Rituximab (Rituxan®); National Government Services, Inc. (MAC Part B) (13102, 13202) - Connecticut, New York 08/13/2012
13. A47797 Local Coverage Article for Approved Drugs and Biologicals; Includes Cancer Chemotherapeutic Agents; Novitas Solutions (MAC Part B) (12402) New Jersey. 08/13/2012
Q2043 Sipuleucel- T (Provenge®)

I. Prostate Cancer- Adenocarcinoma (185, V10.46)
   A. Castration - recurrent metastatic disease
   B. Asymptomatic or minimally symptomatic with
      1. Performance status 0-1, and
      2. A life expectancy of greater than 6 months, and
      3. No visceral disease
   C. Limited to one (1) treatment regimen in a patient’s lifetime, consisting of three (3) doses with
      each dose administered approximately two (2) weeks apart for a total treatment period not to
      exceed 30 weeks from the first administration¹,²

References

1. Prescribing Information PROVENGE® (Sipuleucel-T) Suspension for intravenous Infusion. Dendreon Corporation, 3005 First Avenue,
   Seattle, WA 98121. Accesses 08/13/2012
2. AS1280, Autologous Cellular Immunotherapy Treatment of Metastatic Prostate Cancer (MAC- Part B): CGS Administrators, LLC (15202);
   Accessed 08/13/2012
3. Retired.
5. National Comprehensive Cancer Network (NCCN) NCCN Drugs & Biologics Compendium™ Sipuleucel-T Provenge®
   www.nccn.org, Accessed 08/13/2012
J9351  Topotecan; Topotecan HCl (Hycamtin®Injection)

I.  Bone Cancer
   A.  Ewing’s Sarcoma; Mesenchymal chondrosarcoma (170.0-170.9, V10.81)
      1.  Used in combination with cyclophosphamide with or without vincristine and growth factor support for
          a.  Relapse with or without radiation therapy
          b.  Progressive disease following primary treatment
   B.  Osteosarcoma (170.0-170.9, V10.81)
      1.  Second line therapy in combination with cyclophosphamide and growth factor support

II.  Central Nervous System Cancers
   A.  Brain Metastases
      1.  Limited brain metastases (1-3) metastatic lesions (198.3, V10.11)
          a.  Single-agent treatment for brain metastases if active against primary tumor (lung)
              i.  Primary treatment for disseminated systemic disease with poor systemic treatment options for recurrent disease
      2.  Multiple (>3) metastatic lesions brain metastases (198.3, V10.11)
          a.  Single-agent treatment if active against primary tumor (lung) for brain metastases in patients with recurrent stable systemic disease
   B.  Primary central nervous system lymphoma (200.50, 200.51)
      1.  Single agent treatment for progressive disease in patients who have received prior methotrexate-based regimen without prior radiation therapy
          a.  After prolonged response to prior regimen in combination with radiation therapy after short or no response to prior regimen
      2.  Consider systemic treatment for progressive or recurrent disease in patients with prior whole brain radiation therapy

III. Cervical Cancer (Adenocarcinoma; Squamous Cell Carcinoma) (180.0, 180.1, 180.8, 180.9, V16.49) (5) (NCCN 2A)
   A.  First-line therapy in combination with cisplatin for local/regional recurrence distant metastases or second line if not given first line (clarification of policy)

IV.  Chronic Myelomonocytic Leukemia (CMML) (205.10, 205.11, 205.12)2,4

V.  Myelodysplastic Syndrome (MDS) (238.72-238.76)2,4

VI. Non-Melanoma Skin Cancers- Merkel Cell Carcinoma (209.31-209.36, 209.75, V10.91)
   A.  Treatment for distant metastatic disease or disseminated recurrence

VII. Ovarian Cancer (Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer) (158.8, 183.0, 183.2-183.5, 183.8, 183.9, V10.43)
A. Preferred single-agent recurrence therapy, if platinum resistant, for
   1. Recurrence as evidenced by findings other than serially rising CA-125 levels in patients
      who have received prior chemotherapy (5) (Treatment based on CA 125 alone are NCCN
      2B)
   2. Progressive, stable, or persistent disease on primary chemotherapy
   3. Relapse after complete remission following primary chemotherapy
B. Stage II-IV disease showing partial response to primary treatment

VIII. Small Cell Lung Cancer (SCLC) (162.0, 162.2-162.5, 162.8, 162.9, 197.0, 198.3,
     198.5, V10.11)
   A. Subsequent chemotherapy as a single agent for
      1. Relapse within 6 months following complete or partial response with initial treatment
         primary progressive disease (performance status 0-2)
         a. For relapse during 2 to 6 months
         b. For relapse less than 2 months

IX. Endometrial cancer 182.0-182.8 (4)

X. Essential thrombocythemia - myelofibrosis with myeloid metaplasia 238.71 -
   238.76 (6)

References

1. Prescribing Information, Hycamtin® (topotecan) capsules GlaxoSmithKline. Research Triangle Park, NC 27709, Available at:  
3. L26746, Drugs and Biologicals- Chemotherapeutic- 4I-92AB-R31, MAC- Part B: Trail Blazer Health Enterprises, LLC (04402) Texas  
   Accessed 08/13/2012
4. L28576, Chemotherapy Drugs and their Adjuncts (MAC- Part B): Wisconsin Physicians Service Insurance Corporation (05102, 5302, 
5. National Comprehensive Cancer Network (NCCN) NCCN Drugs & Biologics Compendium™ Topotecan (Hycamtin®) Available at  
   Accessed 8/13/2012
I. Breast Cancer- Invasive (174.0-174.6, 174.8, 174.9, 175.0, 175.9)
   A. Preoperative therapy in combination with paclitaxel followed by FEC/CEF (fluorouracil, epirubicin, and cyclophosphamide) regimen for patients with human epidermal growth factor receptor 2 (HER2)-positive, stage IIA, IIB, or T3, N1, M0 disease who desire breast preservation and fulfill criteria for breast-conserving surgery except for tumor size or for patients with locally advanced disease (stage IIIA, IIIB, or IIIC)
   B. Adjuvant therapy for human epidermal growth factor receptor 2 (HER2)-positive, stage I, IIA, IIB, or T3, N1, M0 disease (ductal, lobular, mixed, or metaplastic histologies) that is pN0 (tumor greater than 0.5 cm), pN1mi, or node-positive or for patients with locally advanced disease (stage IIIA, IIIB, or IIIC)
      1. Concurrently with paclitaxel following AC (doxorubicin and cyclophosphamide) regimen as preferred regimen
      2. In TCH (docetaxel, carboplatin, and trastuzumab) regimen as preferred regimen
      3. In combination with docetaxel followed by FEC/CEF (fluorouracil, epirubicin, and cyclophosphamide) regimen
      4. Following chemotherapy
      5. In combination with docetaxel following AC regimen
   C. Used in combination with aromatase inhibition for the treatment of recurrent or stage IV estrogen receptor-positive, human epidermal growth factor receptor 2 (HER2) positive disease in postmenopausal women* who have received no prior endocrine therapy within one year
   D. Preferred regimen for patients with human epidermal growth factor receptor 2 (HER2)-positive recurrent or metastatic breast cancer that is hormone receptor-negative or hormone receptor-positive and endocrine therapy refractory and not characterized by bone or soft tissue involvement only or asymptomatic visceral disease as
      1. First-line therapy in combination with docetaxel, vinorelbine, or capecitabine or with paclitaxel with or without carboplatin
      2. Treatment for trastuzumab-exposed HER2-positive disease in combination with lapatinib without cytotoxic therapy, with docetaxel, vinorelbine, or capecitabine, or with paclitaxel with or without carboplatin

* Men with breast cancer should be treated similarly to postmenopausal women, except that use of an aromatase inhibitor is ineffective without concomitant suppression of testicular steroidogenesis

II. Esophageal and Esophagogastric Junction Cancers (Adenocarcinoma) (150.0-150.5, 150.8, 150.9, 151.0, 235.5)
   A. Used in combination with systemic chemotherapy (with cisplatin and fluorouracil or capecitabine) for the treatment of patients with advanced HER2-neu protein over expressing gastric adenocarcinoma

III. Gastric Cancer (Adenocarcinoma) (151.0-151.6, 151.8, 151.9, 235.2)
A. Used in combination with systemic cisplatin and fluorouracil or capecitabine chemotherapy for the treatment of patients with advanced HER2-neu protein over expressing gastric adenocarcinoma

References

3. Retired
4. L29297, Topotecan Trastuzumab (Herceptin®), MAC- Part B: First Coast Service Options, Inc. (MAC - Part B) (09102) Florida. Accessed 8/14/2012