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Abraxane® (paclitaxel protein-bound particles for injectable suspension) J9264

When requesting Abraxane® (paclitaxel protein-bound particles for injectable suspension) the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**¹

- Breast cancer - recurrent or metastatic
- Non-small cell lung cancer (NSCLC) - advanced or metastatic
- Pancreatic adenocarcinoma

**Approved Off-label Compendial uses**²⁻⁴

- Anal cancer²
- Cervical cancer - recurrent or metastatic³
- Head and neck cancer²
- Melanoma²⁻³
- NSCLC - may be substituted for either paclitaxel or docetaxel in individuals who have experienced hypersensitivity reactions after receiving paclitaxel or docetaxel despite premedication or for individuals in whom standard hypersensitivity premedication are contraindicated.²⁻³
- Ovarian cancer²⁻³
  - Epithelial ovarian cancer
  - Fallopian tube cancer
  - Primary peritoneal cancer

**Coverage Guidelines**

For all indications:
- Do not administer Abraxane® (paclitaxel protein-bound particles for injectable suspension) therapy to individuals with baseline neutrophil counts of less than 1,500 cells/mm³.¹

**Breast cancer - recurrent or metastatic**²

**Non-Small Cell Lung Cancer (NSCLC)**²

- Advanced or metastatic
- May be substituted for either paclitaxel or docetaxel in patients who have experienced hypersensitivity reactions after receiving paclitaxel or docetaxel despite premedication or for patients in whom standard hypersensitivity premedications are contraindicated.
Pancreatic adenocarcinoma

Anal Cancer

Cervical cancer - recurrent or metastatic

Head and neck cancer

Melanoma

Ovarian cancer - epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer

Additional Information for Prescribers

- It is recommended that frequent peripheral blood cell counts be performed to monitor the occurrence of bone marrow suppression.

References

3. National Comprehensive Cancer Network Drugs & Biologics Compendium (NCCN Compendium®) Accessed February 10, 2016. [http://www.nccn.org/professionals/drug_compendium/content/contents.asp](http://www.nccn.org/professionals/drug_compendium/content/contents.asp). Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™). ©2016 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org.
Actemra® (tocilizumab) Injection J3262

When requesting Actemra® (tocilizumab), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-approved indications

Rheumatoid Arthritis (RA)
- An adult with moderately- to severely-active rheumatoid arthritis who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs)

Polyarticular Juvenile Idiopathic Arthritis (PJIA)
- An individual 2 years of age and older with active polyarticular juvenile idiopathic arthritis

Systemic Juvenile Idiopathic Arthritis (SJIA)
- An individual 2 years of age and older with active systemic juvenile idiopathic arthritis

Approved Off-label Compendial uses
- No off-label uses meet evidence standards

Coverage Guidelines

For all indications:
- The individual does not have an active infection (including active tuberculosis or any clinically important localized infection)
- Actemra® (tocilizumab) will not be used in combination with another biologic agent
- For Actemra® (tocilizumab) re-authorization request, the individual's condition must have improved or stabilized with at least 6 months of therapy
- For Actemra® (tocilizumab) initial request, the individual has been screened for latent TB. For positive latent TB, individual must have started/completed or will be treated for TB prior to starting Actemra® (tocilizumab)

Rheumatoid Arthritis (initial authorization)
The individual meets one of the following for approval:
- Had an inadequate response or intolerance to prior biologic agent or
- The disease is moderately- to severely-active and had an inadequate response or intolerance (including contraindication) to at least one non-biologic DMARD or
- Has poor prognostic features (i.e. functional limitation, extraarticular disease, positive rheumatoid factor or anti-cyclic citrullinated peptide antibodies, or bony erosions by radiograph) and had an inadequate response or intolerance (including contraindication) to at least one non-biologic DMARD
Polyarticular Juvenile Idiopathic Arthritis (initial authorization)\textsuperscript{3,5}

The individual meets \textbf{one} of the following for approval:

- Had an inadequate response or intolerance to prior biologic agent \textbf{or}
- Had an inadequate response or intolerance (including contraindication) to at least one non-biologic DMARD

Systemic Juvenile Idiopathic Arthritis (initial authorization)\textsuperscript{4}

The individual meets \textbf{one} of the following for approval:

- Had an inadequate response or intolerance to prior biologic agent \textbf{or}
- With active systemic features (i.e. fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, or serositis), must have an inadequate response or intolerance (including contraindication) to glucocorticoids or non-steroid anti-inflammatory drugs (NSAIDs) \textbf{or}
- Had an inadequate response or intolerance (including contraindication) to methotrexate or leflunomide

\textbf{Additional Information for Prescribers}\textsuperscript{1}

- Serious infections leading to hospitalization or death including tuberculosis (TB), bacterial, invasive fungal, viral, and other opportunistic infections have occurred in individuals receiving Actemra\textsuperscript{®} (tocilizumab) (\textbf{Black Box Warning})
- Must perform test for latent TB; if positive, must start treatment for TB prior to starting Actemra\textsuperscript{®} (tocilizumab) (\textbf{Black Box Warning})
- *The individual must be monitored for active TB during treatment, even if initial latent TB test is negative (\textbf{Black Box Warning})
- *Actemra\textsuperscript{®} (tocilizumab) should be used with caution in an individual who may be at increased risk for GI perforation
- *Avoid use of live vaccines (e.g., FluMist\textsuperscript{®}, oral polio vaccine [OPV], rotavirus, typhoid, yellow fever, measles, varicella, herpes zoster) concurrently with Actemra\textsuperscript{®} (tocilizumab)

* Prescribers are alerted to this safety concern via educational points in the program.

\textbf{References}

Alimta® (pemetrexed) J9305

When requesting Alimta® (pemetrexed), the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

FDA-approved indications¹

- Malignant pleural mesothelioma (MPM)
- Non-small cell lung cancer (NSCLC)

Approved Off-label Compendial uses²,³

- Bladder cancer²
  - Primary carcinoma of urethra
  - Upper GU tract tumors
  - Urothelial carcinoma of prostate
- Central nervous system cancers - primary CNS lymphoma²
- Cervical cancer²/Ovarian cancer²
  - Epithelial ovarian cancer
  - Fallopian tube cancer
  - Primary peritoneal cancer
- Thymomas and thymic carcinomas²

Coverage Guidelines²

**Malignant Pleural Mesothelioma²**
- Induction therapy in combination with cisplatin for medically operable disease
- Single agent or in combination with cisplatin, carboplatin, or bevacizumab and cisplatin
- Second-line therapy or beyond as a single agent

**Non-Small Cell Lung Cancer (NSCLC)²**
- Preoperative concurrent chemoradiation in combination with cisplatin or carboplatin
- In combination with cisplatin as induction chemotherapy or neoadjuvant chemotherapy
- Initial treatment as definitive concurrent chemoradiation in combination with carboplatin or cisplatin
- Adjuvant chemotherapy in combination with cisplatin
- Adjuvant concurrent chemoradiation or concurrent chemoradiation in combination with cisplatin or carboplatin
- Treatment for recurrence of metastases as a single agent and with or without bevacizumab and/or in combination with cisplatin or carboplatin
- Single agent (if not already given) as subsequent therapy for metastatic disease
Bladder cancer - primary carcinoma of urethra/upper GU tract tumors/urothelial carcinoma of prostate
- Second-line therapy or beyond as a single agent for metastatic disease

Central nervous system cancers - primary CNS lymphoma
- Single agent therapy for progressive or recurrent disease

Cervical cancer
- Second-line therapy or beyond as a single agent for local/regional recurrence or distant metastases

Ovarian cancer - epithelial ovarian cancer/fallopian tube cancer/ primary peritoneal cancer
- Single agent therapy for persistent or recurrent disease

Thymomas and thymic carcinomas
- Second-line therapy or beyond

Additional Information for Prescribers
- None

References
2. National Comprehensive Cancer Network Drugs & Biologics Compendium (NCCN Compendium®) Accessed February 11, 2016. http://www.nccn.org/professionals/drug_compendium/content/contents.asp. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™). ©2016 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org

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Avastin® (bevacizumab) J9035

When requesting Avastin® (bevacizumab), the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**

- Brain or central nervous system cancers
  - Glioblastoma
- Cervical cancer
- Colorectal cancer
- Kidney cancer
- Non-small cell lung cancer
- Ovarian cancer

**Approved Off-label Compendial uses**

- Brain or central nervous system cancers
  - Adult intracranial and spinal ependymoma (excludes subependymoma)
  - Anaplastic gliomas
- Breast cancer
- Intravitreal therapy for non-oncology indications
  - Choroidal neovascular (wet) age-related macular degeneration
  - Macular edema secondary to:
    - Diabetes
    - Branch retinal vein occlusion or Central retinal vein occlusion
  - Proliferative diabetic retinopathy
  - Neovascular glaucoma
  - Choroidal retinal neovascularization secondary to:
    - Pathologic myopia
- Mesothelioma
- Soft tissue sarcoma
- Uterine cancer

**Coverage Guidelines**

**Brain or Central Nervous system cancers**

- Adult intracranial and spinal ependymoma (excludes subependymoma)
  - As single agent treatment for disease progression
- Anaplastic gliomas
  - Treatment of recurrent disease
- Glioblastoma

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Treatment of progressive or recurrent disease\(^1,2\)

**Breast Cancer**\(^2\)
- In combination with paclitaxel for individuals with recurrent or metastatic disease that is\(^2\):
  - HER2 Negative\(^2\)
    - There is evidence of rapid progression of disease in any organs (symptomatic visceral disease or visceral crisis) including: lymphangitic lung metastases, bone marrow replacement, carcinomatous meningitis, or significant liver metastases\(^2,3\) or
    - Either hormone receptor- negative or hormone receptor positive and endocrine (hormone) therapy refractory (eg, tamoxifen, raloxifene, anastrozole, etc.)\(^2\)

**Cervical Cancer**\(^2\)
- Treatment of local/regional recurrence or distant metastases\(^2\)

**Colorectal cancer**\(^1,2\)
- Adenocarcinoma histology\(^2\) and
- The individual has advanced, metastatic or unresectable disease\(^2\) and
- Avastin\(^\circledast\) (bevacizumab) will be used\(^2\):
  - In combination with capecitabine, FOLFOX (fluorouracil, leucovorin, and oxaliplatin), FOLFIRI (fluorouracil, leucovorin, and irinotecan), CapeOx (capecitabine and oxaliplatin), FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan), 5-FU/leucovorin, irinotecan, or irinotecan/oxaliplatin\(^2\)

**Intravitreal therapy for non-oncology indications**\(^4\)
- Choroidal neovascular (wet) age-related macular degeneration\(^4\)
- Macular edema secondary to\(^4\):
  - Diabetes\(^4\)
  - Branch retinal vein occlusion\(^4\) or
  - Central retinal vein occlusion\(^4\)
- Proliferative diabetic retinopathy\(^4\)
- Neovascular glaucoma\(^4\)
- Choroidal retinal neovascularization secondary to\(^4\)
  - Pathologic myopia\(^4\)

**Kidney Cancer**\(^1,2\)
- For relapsed or for surgically unresectable stage IV disease\(^2\)

**Mesothelioma**\(^2\)
- Malignant pleural disease\(^2\)
**Non-Small Cell Lung Cancer**
- Non-squamous cell histology and
- For unresectable, recurrent or metastatic disease and
- Performance status 0-1

**Ovarian Cancer**
- Epithelial Ovarian Cancer/ Fallopian Tube Cancer/Primary Peritoneal Cancer
  - For recurrent or persistent disease
- Sex cord/stromal tumors
  - Clinical relapse in individuals with stage II-IV granulosa cell tumors

**Soft tissue sarcoma**
- Angiosarcoma
- Solitary fibrous tumor
- Hemangiopericytoma

**Uterine cancer**
- Endometrial carcinoma
  - For progressed disease

---

**Additional Information for Prescribers**

**Boxed Warning: Gastrointestinal perforations, surgery and wound healing complications, and hemorrhage**
- * Gastrointestinal perforation: occurs in up to 3.2% of Avastin (bevacizumab) treated individuals. Discontinue Avastin (bevacizumab) for gastrointestinal perforation.
- * Surgery and wound healing complications: discontinue in individuals with wound dehiscence. Discontinue at least 28 days prior to elective surgery. Do not initiate Avastin (bevacizumab) for at least 28 days after surgery and until the surgical wound is fully healed.
- * Hemorrhage: severe or fatal hemorrhage, hemoptysis, gastrointestinal bleeding, CNS hemorrhage, and vaginal bleeding are increased in Avastin (bevacizumab) treated individuals. Do not administer Avastin (bevacizumab) to individuals with serious hemorrhage or recent hemoptysis.

* Prescribers are alerted to the above safety concerns via educational points in the program.

**References**

Benlysta® (belimumab) J0490

When requesting Benlysta® (belimumab), the individual requiring treatment must be diagnosed with the following FDA-approved indication and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indication**

- For the treatment of an adult with active, autoantibody-positive, systemic lupus erythematosus who is receiving standard therapy

**Approved Off-label Compendial uses**

- None

**Coverage Guidelines**

- Active systemic lupus erythematosus (SLE)
- The individual is autoantibody (e.g., antinuclear antibody test [ANA], antibodies to double-stranded DNA [anti-dsDNA], antibodies to Sm [anti-Sm]) positive
- The individual does not have severe active lupus nephritis or severe active central nervous system lupus
- Benlysta® (belimumab) will not be used in combination with other biologics or intravenous cyclophosphamide
- The individual is receiving standard therapy for SLE including any of the following (alone or in combination):
  - Corticosteroids
  - Antimalarials
  - Nonsteroidal anti-inflammatory drugs (NSAIDs)
  - Immunosuppressive agents
- The individual is 18 years of age or older

Benlysta® (belimumab) dosing 10 mg/kg at 2 week intervals for the first 3 doses and at 4 week intervals thereafter.

**Additional Information for Prescribers**

**Limitations of Use**

The efficacy of Benlysta® (belimumab) has not been evaluated in individuals with severe active lupus nephritis or severe active central nervous system lupus. Benlysta® (belimumab) has not been studied in combination with other biologics or intravenous cyclophosphamide. Use of Benlysta® (belimumab) is not recommended in these situations.
## References

   http://www.micromedexsolutions.com
Doxil® (doxorubicin hydrochloride liposome injection) Q2050

When requesting Doxil® (doxorubicin hydrochloride liposome injection), the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

FDA-approved indications

- AIDS-related Kaposi’s Sarcoma
- Ovarian cancer
- Multiple myeloma

Approved Off-label Compendial uses

- Breast cancer
- Dermatofibrosarcoma protuberans
- Fallopian tube cancer
- Hodgkin lymphoma
  - Classical Hodgkin lymphoma
  - Nodular lymphocyte-predominant Hodgkin lymphoma
- Non-Hodgkin lymphoma (NHL)
  - Adult T-cell leukemia/lymphoma
  - Castleman’s disease
  - Diffuse large B-cell lymphoma
  - Mycosis Fungoides/Sezary Syndrome
  - Nongastric MALT lymphoma
  - Peripheral T-cell lymphoma
  - Primary cutaneous B-cell lymphoma
  - Primary cutaneous CD30+ T-cell lymphoproliferative disorders
- Primary peritoneal cancer
- Soft tissue sarcoma
  - Angiosarcoma
  - Desmoid tumors (aggressive fibromatosis)
  - Retroperitoneal/intra-abdominal
  - Rhabdomyosarcoma
  - Soft tissue sarcoma of the extremity/superficial trunk, head/neck
- Uterine cancer
  - Endometrial carcinoma
  - Uterine sarcoma
**Coverage Guidelines**

**AIDS-related Kaposi’s Sarcoma**
- For individuals who had failure or intolerance to prior systemic chemotherapy

**Breast Cancer**
- For treatment of individuals with recurrent or metastatic disease

**Dermatofibrosarcoma protuberans**

**Fallopian Tube Cancer**

**Hodgkin’s Lymphoma**
- Classical Hodgkin’s lymphoma
  - For treatment of individuals who have been previously treated with other chemotherapy and have refractory or relapsed disease
- Lymphocyte-predominant Hodgkin’s lymphoma
  - For treatment of individuals who have been previously treated with other chemotherapy and have refractory or relapsed disease

**Multiple Myeloma/Solitary Plasmacytoma**
- For treatment of individuals with active (symptomatic) myeloma

**Non-Hodgkin’s Lymphoma**
- Adult T-Cell Leukemia/Lymphoma
- Castleman’s Disease
- Diffuse Large B-Cell Lymphoma
- Mycosis Fungoides/Sezary Syndrome
- Nongastric MALT Lymphoma
- Peripheral T-Cell Lymphoma
- Primary Cutaneous B-Cell Lymphoma
- Primary Cutaneous CD30+ T-Cell Lymphoproliferative Disorders

**Ovarian Cancer**

**Primary Peritoneal Cancer**
- Soft Tissue Sarcoma
- Angiosarcoma
- Desmoid Tumor (Aggressive Fibromatosis)
- Retroperitoneal/Intrabdominal
- Rhabdomyosarcoma

**Soft Tissue Sarcoma of Extremity/Superficial Trunk, Head/Neck**

**Uterine Cancer**
• Endometrial Carcinoma
• Uterine Sarcoma

Additional Information for Prescribers

- Doxil® (doxorubicin hydrochloride liposome injection) can cause myocardial damage, including congestive heart failure, as the total cumulative dose of doxorubicin hydrochloride approaches 550 mg/m$^2$. The risk of cardiomyopathy may be increased at lower cumulative doses in individuals with mediastinal irradiation.
- Acute infusion-related reactions occurred in 11% of patients with solid tumors treated with Doxil® (doxorubicin hydrochloride liposome injection). Serious, life-threatening and fatal infusion reactions have been reported. Medications/emergency equipment to treat such reactions should be available for immediate use.

References

2. National Comprehensive Cancer Network Drugs & Biologics Compendium (NCCN Compendium®) Accessed June 1, 2016. http://www.nccn.org/professionals/drug_compendium/content/contents.asp. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™). ©2016 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org

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Entyvio® (vedolizumab) injection J3590; C9026

When requesting Entyvio® (vedolizumab), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**

- Ulcerative colitis
- Crohn’s disease

**Approved Off-label Compendial uses**

- No off-label uses meet evidence standards

### Coverage Guidelines

#### Ulcerative colitis and Crohn’s disease

**Initial authorization:**
The individual meets all of the following criteria for approval:

- Has moderately- to severely-active disease
- Is 18 years of age or older
- Had an inadequate response with, lost response to, or was intolerant to a tumor necrosis factor (TNF) blocker (e.g., infliximab [Remicade®], adalimumab [Humira®], certolizumab pegol [Cimzia®]) or an immunomodulator (e.g. azathioprine, cyclosporine, methotrexate)

and

- Had an inadequate response with, was intolerant to, or demonstrated dependence on corticosteroids

**Approval duration: 14 weeks**

**Reauthorization:**
The individual must have shown evidence of therapeutic benefit by week 14 of therapy for approval.
Additional Information for Prescribers

Ulcerative colitis and Crohn’s disease

The individual should be up to date with all immunizations before initiating treatment with Entyvio® (vedolizumab).

- Live vaccines (e.g., typhoid, yellow fever, herpes zoster, FluMist®) may be administered concurrently with Entyvio® (vedolizumab) only if the benefits outweigh the risks
- Treatment with Entyvio® (vedolizumab) is not recommended in an individual with active, severe infection until the infection is controlled. The individuals should be screened for tuberculosis (TB)
- Another integrin receptor antagonist has been associated with progressive multifocal leukoencephalopathy (PML). While on Entyvio® (vedolizumab), an individual should be monitored for any new onset or worsening of neurological signs and symptoms
- Entyvio® (vedolizumab) should be discontinued in an individual with jaundice or other evidence of significant liver disease. The individual should be monitored for signs or symptoms of liver injury, including elevations in liver transaminases (AST, ALT) and total bilirubin

Prescribers are alerted to these safety concerns via educational points in the program.

References

Erbitux® (cetuximab) J9055

When requesting Erbitux® (cetuximab), the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

FDA-approved indications

- Colon cancer
- Head and neck cancer
- Rectal cancer

Approved Off-label Compendial uses

- Non-melanoma skin cancer - squamous cell skin cancer
- Non-small cell lung cancer (NSCLC)
- Penile cancer

Coverage Guidelines

Colon cancer

- Adenocarcinoma histology
- Tumors express KRAS/NRAS wild-type gene
- Disease is unresectable advanced or metastatic
- Individual has not previously failed treatment or experienced disease progression with either Erbitux® (cetuximab) or Vectibix® (panitumumab)
- Erbitux® (cetuximab) will be administered:
  - In combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin), FOLFIRI (fluorouracil, leucovorin, and irinotecan) or irinotecan OR
  - As a single agent for individuals who experienced disease progression after prior treatment with fluoropyrimidine- [i.e. capecitabine (Xeloda), fluorouracil (5-FU)], oxaliplatin- (Eloxatin), and irinotecan- (Camptosar) containing regimen OR had an intolerance to intensive therapy (i.e., FOLFOX, FOLFIRI)

Head and neck cancer

Non-melanoma skin cancer - squamous cell skin cancer

- Regional recurrence or distant metastases

Non-small cell lung cancer (NSCLC)

- Metastatic disease
- Individual progressed on epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) therapy (e.g., erlotinib, gefitinib, or afatinib)
- Erbitux® (cetuximab) will be used in combination with Gilotrif® (afatinib)
Penile cancer
- Second line treatment of metastatic disease
- Erbitux® (cetuximab) used as a single agent

Rectal cancer
- Adenocarcinoma histology
- Tumors express KRAS/NRAS wild-type gene
- Disease is unresectable advanced or metastatic
- Individual has not previously failed treatment or experienced disease progression with either Erbitux® (cetuximab) or Vectibix® (panitumumab)
- Erbitux® (cetuximab) will be administered:
  - In combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin), FOLFIRI (fluorouracil, leucovorin, and irinotecan) or irinotecan OR
  - As a single agent
    - Individual experienced disease progression after prior treatment with fluoropyrimidine- [i.e. capecitabine (Xeloda), fluorouracil (5-FU)], oxaliplatin- (Eloxatin), and irinotecan- (Camptosar) containing regimen
    - OR had an intolerance to intensive therapy (i.e., FOLFOX, FOLFIRI)

Additional Information for Prescribers

- The following are important safety concerns regarding the use of Erbitux® (cetuximab):
  - Serious infusion reactions occurred with the administration of Erbitux in approximately 3% of patients in clinical trials, with fatal outcome reported in less than 1 in 1000. Immediately interrupt and permanently discontinue Erbitux infusion for serious infusion reactions.
  - Cardiopulmonary arrest and/or sudden death occurred in 2% of patients with squamous cell carcinoma of the head and neck treated with Erbitux and radiation therapy in Study 1 and in 3% of patients with squamous cell carcinoma of the head and neck treated with European Union (EU)-approved cetuximab in combination with platinum-based therapy with 5-fluorouracil (5-FU) in Study 2. Closely monitor serum electrolytes, including serum magnesium, potassium, and calcium, during and after Erbitux administration.

References

2. National Comprehensive Cancer Network Drugs & Biologics Compendium (NCCN Compendium®) Accessed September 1, 2016. http://www.nccn.org/professionals/drug_compendium/content/contents.asp Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™). ©2016 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org.

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Eylea® (aflibercept) Injection J0178; Q2046

When requesting Eylea® (aflibercept), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**¹

- Neovascular (wet) age-related macular degeneration (AMD)
- Macular edema following retinal vein occlusion (RVO)
- Diabetic macular edema (DME)
- Diabetic retinopathy (DR) in patients with DME

**Approved Off-label Compendial uses**²,³,⁴

- None

**Coverage Guidelines**¹

For all approved indications the individual meets both of the following criteria for approval

B. Does not have ocular or periocular infection

C. Does not have active intraocular inflammation

**Additional Information for Prescribers**¹

- None

**References**

3. Local Coverage Determination (L33394) A52451 related to LCD (MAC-Part B) (CT, IL, MA, ME, MN, NH, NY, RI, VT, WI); National Government Services, Inc. Accessed November 13, 2015. [https://www.cms.gov/medicare-coverage-database/search/search-results.aspx?SearchType=Advanced&CoverageSelection=Local&PolicyType=Final&s=All&CntrctrType=12%7c9&KeyWord=Drugs+and+Biologics%2c+Coverage+of%2c+for+Label+and+Off-Label+Uses&KeyWordLookUp=Title&KeyWordSearchType=Exact&kq=true&bc=IAAAAAAAAAAAAA%3d%3d&](https://www.cms.gov/medicare-coverage-database/search/search-results.aspx?SearchType=Advanced&CoverageSelection=Local&PolicyType=Final&s=All&CntrctrType=12%7c9&KeyWord=Drugs+and+Biologics%2c+Coverage+of%2c+for+Label+and+Off-Label+Uses&KeyWordLookUp=Title&KeyWordSearchType=Exact&kq=true&bc=IAAAAAAAAAAAAA%3d%3d&)
4. Local Coverage Determination (L34741) Drugs and Biologics (Non-chemotherapy) (MAC-Part B) (IA, IN, KS, MI, MO, NE); Wisconsin Physicians Service Insurance Corporation. Accessed November 13, 2015. [https://www.cms.gov/medicare-coverage-database/search/search-results.aspx?SearchType=Advanced&CoverageSelection=Local&PolicyType=Final&s=20%7c17%7c21%7c27%7c29%7c36&CntrctrType=13%7c12%7c9&KeyWord=drugs+and+biologics&KeyWordLookUp=Title&KeyWordSearchType=Exact&kq=true&bc=IAAAAAAAAAAAAA%3d%3d&](https://www.cms.gov/medicare-coverage-database/search/search-results.aspx?SearchType=Advanced&CoverageSelection=Local&PolicyType=Final&s=20%7c17%7c21%7c27%7c29%7c36&CntrctrType=13%7c12%7c9&KeyWord=drugs+and+biologics&KeyWordLookUp=Title&KeyWordSearchType=Exact&kq=true&bc=IAAAAAAAAAAAAA%3d%3d&)

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Gemzar<sup>®</sup> (gemcitabine) J9201

When requesting Gemzar<sup>®</sup> (gemcitabine), the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications<sup>1</sup>**

- Breast Cancer
- Non-small Cell Lung Cancer
- Ovarian Cancer
- Pancreatic Cancer

**Approved Off-label Compendial uses<sup>2,3</sup>**

- Bladder Cancer
- Bone Cancer
- Head & Neck Cancer
- Hepatobiliary Cancers
- Hodgkin’s Lymphoma
- Malignant Pleural Mesothelioma
- Non-Hodgkin’s Lymphoma
- Occult Primary
- Small Cell Lung Cancer (SCLC)
- Soft Tissue Sarcoma
- Testicular Cancer
- Thymomas and Thymic Carcinomas
- Uterine Sarcoma
- Cervical cancer
- Kidney cancer
- Non-melanoma skin cancer

**Coverage Guidelines<sup>1-3</sup>**

**Bladder Cancer<sup>2</sup>**
- Gemcitabine is used as a single agent or in combination with cisplatin

**Bone Cancer<sup>2</sup>**
- Ewing’s sarcoma
  - Disease is relapsed, progressive or metastatic
  - Gemcitabine is used in combination with docetaxel
• Osteosarcoma\(^2\)
  - Second-line therapy as a single agent or in combination with docetaxel

**Breast Cancer\(^1,2\)**
- Disease is invasive
- Disease is recurrent or metastatic
- Disease is characterized as symptomatic visceral disease/visceral crisis OR refractory to endocrine therapy
- For HER-2 negative disease, gemcitabine is used as a single agent or in combination with paclitaxel or carboplatin
- For HER-2 positive disease, gemcitabine is used in combination with trastuzumab and patient has previoulsy been exposed to trastuzumab

**Cervical Cancer\(^2\)**
- Disease is recurrent or metastatic
- Use as a second-line of therapy
- Gemcitabine is used as a single agent

**Head & Neck Cancer\(^2\)**
- Primary cancer site is nasopharynx
- For primary therapy request, gemcitabine is used in combination with cisplatin
- For very advanced cancer: 1) for performance status 0-1, gemcitabine is used as a single agent or in combination with cisplatin or vinorelbine, 2) for performance status 2, gemcitabine is used as a single agent

**Hepatobiliary Cancers\(^2\)**
- Extrahepatic cholangiocarcinoma/Intrahepatic cholangiocarcinoma
  - Disease status is resected, unresectable, or metastatic
  - Gemcitabine is used as a single agent or in combination with capecitabine, oxaliplatin, or cisplatin as:
- Gallbladder cancer
  - For unresectable or metastatic disease, gemcitabine is used as a single agent or in combination with capecitabine, oxaliplatin, or cisplatin
  - For resected disease, gemcitabine is used a single agent

**Hodgkin’s Lymphoma\(^2\)**

Classical Hodgkin’s Lymphoma
- For primary treatment request, patient must be over 60 years of age OR disease is relapsed or refractory
- Gemcitabine is used in combination with other chemotherapeutic agents

Nodular lymphocyte-predominant Hodgkin lymphoma
- Disease is relapsed or refractory
• Gemcitabine is used in combination with rituximab and other chemotherapeutic agents

Kidney Cancer²
• For collecting duct or medullary cell histology, gemcitabine is used in combination with carboplatin or cisplatin
• For sarcomatoid histology, disease is relapsed or surgically unresectable stage IV and gemcitabine is used in combination with doxorubicin or sunitinib

Malignant Pleural Mesothelioma²
• First-line or adjuvant therapy request, gemcitabine is used in combination with cisplatin
• Second-line treatment as a single agent

Non-Hodgkin's Lymphoma²

Adult T-cell leukemia/lymphoma:
• Patient had nonsresponse to first line therapy
• If gemcitabine is used as a component of chemotherapy regimen, patient is intended to proceed to transplant

AIDS-related B-cell lymphoma
  • Gemcitabine is used as a component of chemotherapy regimen
  • The request is for second-line of therapy or beyond for AIDS-related diffuse large B-cell lymphoma, primary effusion lymphoma, and lymphoma associated with Castleman’s disease
• Burkitt Lymphoma/Follicular lymphoma/Gastric MALT lymphoma/Mantle cell lymphoma/Splenic marginal zone lymphoma
  • The request is for second-line of therapy or beyond
  • Gemcitabine is used as a component of chemotherapy regimen
• Diffuse large B-cell lymphoma/Extranodal NK-T-cell lymphoma, nasal type/Nongastric MALT lymphoma/Primary cutaneous diffuse large B-cell lymphoma, leg type
  • Gemcitabine is used as a component of chemotherapy regimen
• Mycosis fungoides (MF)/Sezary Syndrome (SS)
  • For stage IB or IIA, there is a histologic evidence of folliculotropic or large cell transformation
  • For stage IIB, patient has generalized extent tumor, transformed, and/or folliculotropic disease
  • Stage III or IV non-Sezary or visceral disease
• Peripheral T-cell Lymphoma
  • Patient has one of the following subtypes: angioimmunoblastic T-cell lymphoma, peripheral T-cell lymphoma not otherwise specified, anaplastic large cell lymphoma, or enteropathy-associated T-cell lymphoma
  • The request is for second-line therapy or beyond
• Primary cutaneous CD30+ T-cell lymphoproliferative disorders
- Patient has primary cutaneous anaplastic large cell lymphoma (ALCL) with multifocal lesions or cutaneous ALCL with regional nodes
- Disease is relapsed or refractory

**Non-Melanoma skin cancer**
- Primary cancer site is dermatofibrosarcoma protuberans (DFSP) and metastatic

**Non-small Cell Lung Cancer**
- Gemcitabine is used in combination with cisplatin if disease is not recurrent or metastatic
- For recurrent or metastatic disease:
  - Performance status is 0-2
  - Gemcitabine is used as a single agent for subsequent therapy for progressive disease or for maintenance therapy
  - For first-line of therapy (PS 0-1), gemcitabine is used in combination with one of the followings: cisplatin, carboplatin, docetaxel, or vinorelbine
  - For first-line of therapy (PS 2), gemcitabine is used as a single agent or in combination with carboplatin, docetaxel, or vinorelbine

**Occult Primary**
- Gemcitabine is used in combination with cisplatin, irinotecan or docetaxel in patients with performance status (PS) 1-2 or PS 0 with aggressive cancer

**Ovarian Cancer**
- Patient has one of the following histopathology: epithelial ovarian/fallopian tube/primary peritoneal, or malignant germ cell tumors
  - For malignant germ cell tumors, disease is recurrent and gemcitabine is used in combination with paclitaxel
  - For epithelial ovarian/fallopian tube/primary peritoneal:
    - Disease is persistent or recurrent
    - For platinum-resistant disease, gemcitabine is used as a single agent
    - For platinum-sensitive disease, gemcitabine is used in combination with cisplatin or carboplatin OR in combination with carboplatin and bevacizumab who have not previously received bevacizumab

**Pancreatic Cancer**
- As a neoadjuvant, adjuvant or induction chemotherapy
- For patients with locally advanced or metastatic disease
- Second-line therapy for patients with progressive disease and good performance status who have received prior fluoropyrimidine-based therapy
Small Cell Lung Cancer (SCLC)²

As a single agent for primary progressive disease or relapsed disease within 6 months following initial treatment with performance status 0-2

Soft Tissue Sarcoma² Retroperitoneal/Intra-abdominal/Angiosarcoma/ Extremity/superficial trunk/Head/Neck/pleomorphic rhabdomyosarcoma:

- Gemcitabine is used as a single agent or in combination with docetaxel or dacarbazine OR with vinorelbine as a palliative chemotherapy

Testicular Cancer²

- As palliative chemotherapy in combination with oxaliplatin and/or paclitaxel

Thymomas and Thymic Carcinomas²

- Second-line therapy as a single agent

Uterine Sarcoma²

- Gemcitabine is used as a single agent or in combination with dacarbazine, vinorelbine, or docetaxel

Additional Information for Prescribers¹

- Gemcitabine is associated with schedule-dependent toxicity. Toxicity is increased with infusion time greater than 60 minutes or dosing more frequently than once weekly.
- Gemcitabine can cause myelosuppression. Myelosuppression should be monitored prior to each cycle and reduce or withhold dose for severe myelosuppression.
- Gemcitabine can cause pulmonary toxicity and respiratory failure. Gemcitabine should be discontinued immediately for unexplained new or worsening dyspnea.
- Gemcitabine can cause hemolytic-uremic syndrome and hepatic toxicity. Renal and hepatic function should be monitored prior to initiation and during therapy
- Gemcitabine can exacerbate radiation therapy toxicity when administered during or within 7 days of radiation therapy.
References


Granix® (tbo-filgrastim) Injection J1446

When requesting Granix® (tbo-filgrastim), the individual requiring treatment must be diagnosed with the following FDA-approved indication and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

**FDA-approved indication**

- For reduction in the duration of severe neutropenia in individuals with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia

**Approved Off-label Compendial uses**

- None

**Coverage Guidelines**

For prophylaxis of chemotherapy-induced febrile neutropenia

- The individual has a solid tumor or non-myeloid malignancy AND
- The individual has experienced febrile neutropenia or dose-limiting neutropenic event with prior chemotherapy cycle OR
- Individual has one of the following risk categories for febrile neutropenia:
  - For high risk for febrile neutropenia:
    - The intent of chemotherapy is curative/adjuvant or to prolong survival OR
    - The intent of chemotherapy is for symptom management. The risk of febrile neutropenia is NOT due to the chemotherapy regimen. If risk of febrile neutropenia is due to the chemotherapy regimen, the use of less myelosuppressive chemotherapy or dose reduction is NOT an option
  - For intermediate risk for febrile neutropenia:
    - The intent of chemotherapy is curative/adjuvant OR
    - The intent of chemotherapy is to prolong survival or to manage symptoms. The risk of febrile neutropenia is NOT due to the chemotherapy regimen. If risk of febrile neutropenia is due to the chemotherapy regimen, the use of less myelosuppressive chemotherapy or dose reduction is NOT an option
  - For low risk of febrile neutropenia, the intent of chemotherapy is curative/adjuvant and individual is at significant risk for serious medical consequences of febrile neutropenia, including death

**Additional Information for Prescribers**

- *Do not administer Granix within 24 hours prior to chemotherapy
* Prescribers are alerted to this safety concern via educational points in the program.

**References**

Herceptin® (trastuzumab) J9355

When requesting Herceptin® (trastuzumab), the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**¹

- Breast cancer
- Gastric or gastroesophageal junction adenocarcinoma

**Approved Off-label Compendial uses**²,³

- Central nervous system cancers
- Esophageal cancer
- Non-small cell lung cancer

**Coverage Guidelines**

**Breast Cancer**¹,²

- Has HER2-positive disease
- For use as neoadjuvant therapy, trastuzumab will be used in combination with chemotherapy
- For adjuvant therapy, trastuzumab can be used in combination with pertuzumab if pertuzumab-containing regimen was not used as neoadjuvant therapy. Otherwise, trastuzumab can be used as a single agent or in combination with other chemotherapy
- For recurrent or metastatic disease, trastuzumab can be used as one of the following: 1) in combination with an aromatase inhibitor if member is a postmenopausal woman and has estrogen receptor-positive disease 2) in combination with pertuzumab and/or other chemotherapy OR 3) as a single agent if member has received one or more chemotherapy regimens for metastatic disease

**Gastric, esophageal and gastroesophageal junction cancer**¹,²

Patient meets ALL of the following criteria
- Has HER2-positive disease
- Disease is advanced or metastatic
- Has not received prior treatment for metastatic disease
- Trastuzumab will be used in combination with chemotherapy

**Central nervous system cancers**²

Has leptomeningeal metastases from breast cancer that is HER-2 positive
Non-small cell lung cancer\(^2,3\)
Has HER-2 positive disease

### Additional Information for Prescribers\(^4\)

- Herceptin can result in cardiac failure manifesting as congestive heart failure (CHF), decreased left ventricular ejection fraction (LVEF), with greatest risk when administered concurrently with anthracyclines. Cardiac function must be evaluated prior to and during treatment. Herceptin should be discontinued for cardiomyopathy.
- Herceptin can cause infusion reactions and pulmonary toxicity. Herceptin should be discontinued for anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome.
- Herceptin can cause embryo-fetal toxicity. Exposure to Herceptin during pregnancy can result in oligohydramnios, in some cases complicated by pulmonary hypoplasia and neonatal death.

### References

2. National Comprehensive Cancer Network Drugs & Biologics Compendium (NCCN Compendium\(^\text{®}\)). Assessed August 29, 2016. [https://www.nccn.org/professionals/drug_compendium/MatrixGenerator/Matrix.aspx?AID=28](https://www.nccn.org/professionals/drug_compendium/MatrixGenerator/Matrix.aspx?AID=28). Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines\(^\text{™}\)). ©2016 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org.
Hycamtin® (topotecan HCl) J9351

When requesting Hycamtin® (topotecan HCl), the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**

- Cervical Cancer
- Ovarian Cancer
- Small Cell Lung Cancer (SCLC)

**Approved Off-label Compendial uses**

- Bone Cancer
  - Ewing’s Sarcoma
  - Osteosarcoma
- Central Nervous System Cancers
- Chronic Myelomonocytic Leukemia (CMML)
- Endometrial cancer
- Myelodysplastic syndrome (MDS)
- Non-Melanoma Skin Cancers- Merkel Cell Carcinoma
- Acute myeloid leukemia (AML)
- Soft tissue sarcoma

**Coverage Guidelines**

For ALL indications:

- Must have baseline neutrophil count greater than or equal to 1,500 cells/mm³ AND baseline platelet count greater than or equal to 100,000 cells/mm³

**Bone Cancer**

- Ewing’s Sarcoma
- Patient meets ALL of the following criteria for approval:
  - Disease is relapsed, progressive or metastatic
  - Use in combination with cyclophosphamide
  - Request is for second line therapy or beyond
- Osteosarcoma
  - For second line therapy in combination with cyclophosphamide
Central Nervous System Cancers
- Leptomeningeal metastases OR
- Limited (1-3)/multiple (>3) metastatic lesions - use as a single agent for recurrent disease AND
- Primary tumor is small cell lung cancer OR
- Primary central nervous system lymphoma
  - Single agent treatment for progressive or recurrent disease

Cervical Cancer
- Disease is recurrent or metastatic
- For first line therapy, must be used in combination with cisplatin or paclitaxel
- For second line therapy, must be used as a single agent

Chronic Myelomonocytic Leukemia (CMML)
- Use as a single agent or in combination with cytarabine

Endometrial cancer
- Use as a single agent

Non-Melanoma Skin Cancers- Merkel Cell Carcinoma
- Has distant metastases or disseminated recurrence

Ovarian Cancer
- Disease is metastatic, persistent or recurrent AND
- Use as a single agent or in combination with Bevacizumab if Bevacizumab has not been given previously

Soft Tissue Sarcoma (STS)
- Has nonpleomorphic rhabdomyosarcoma STS histology AND
- Use as a single agent or in combination with cyclophosphamide

Small Cell Lung Cancer (SCLC)
- Subsequent chemotherapy as a single agent for disease that has relapsed within 6 months following initial treatment or progressive disease on primary therapy

Acute Myeloid Leukemia (AML)
- Use as an induction therapy in combination with cytarabine AND
- Patient is less than 60 years of age
Additional Information for Prescribers

- Hycamtin can cause severe myelosuppression. Hycamtin should be administered to patients with adequate bone marrow reserves. Peripheral blood counts must be monitored and dose be adjusted as needed.
- Hycamtin can cause interstitial lung disease (ILD). Hycamtin should be permanently discontinued for confirmed ILD

References

Immune Globulin Injection J1459, J1556, J1557, J1559, J1561, J1566, J1568, J1569, J1572, J3590

When requesting an immune globulin, the individual requiring treatment must be diagnosed with one of the following FDA-approved or approved off-label compendial requirements and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

The following intravenous immunoglobulin (IVIG) and subcutaneous immunoglobulin (SCIG) products are included in this policy: Bivigam®, Carimune NF®, Flebogamma®, Gammagard®, Gammagard S/D®, Gammaked®, Gammaplex®, Gamunex-C®, Hizentra®, HyQvia®, Octagam®, Privigen®, and Vivaglobin®.

**FDA-approved indications**¹⁻¹²,¹⁸,¹⁹

- Treatment of primary humoral immunodeficiency (e.g., common variable immunodeficiency, X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome, severe combined immunodeficiencies, etc.)
- Idiopathic thrombocytopenia purpura
- Maintenance therapy to improve muscle strength and disability in individuals with multifocal motor neuropathy
- Prevention of bacterial infections in hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell chronic lymphocytic leukemia
- Prevention of coronary artery aneurysms associated with Kawasaki syndrome
- Treatment of chronic inflammatory demyelinating polyneuropathy

Please note: the FDA-approved uses vary based on the respective immune globulin product.

**Approved Off-label Compendial uses**¹³,¹⁴,¹⁶,¹⁷

- Autoimmune diseases
  - Autoimmune hemolytic anemia
  - Autoimmune mucocutaneous blistering disease (i.e., pemphigus vulgaris or pemphigus foliaceus)
  - Autoimmune neutropenia
  - Autoimmune uveitis
  - Dermatomyositis
  - Guillain-Barre syndrome
  - Myasthenia gravis
  - Neonatal jaundice
  - Relapsing-remitting multiple sclerosis
  - von Willebrand disorder
• Infectious and infection related diseases
  ▪ Cytomegalovirus (CMV) induced pneumonitis in solid organ transplants
  ▪ Respiratory syncytial virus
  ▪ Sepsis
  ▪ Toxic shock syndrome
• Secondary immunodeficiencies
  ▪ Multiple myeloma
  ▪ Pediatric human immunodeficiency virus
• Pre- and post transplant
  ▪ Prophylaxis to reduce transplant rejection before transplant
  ▪ Prophylaxis to reduce transplant rejection after transplant
  ▪ Treatment of acute rejection

### Coverage Guidelines

The individual has one of the following diagnoses and meets the criteria for coverage:

- **Autoimmune diseases**
  - Autoimmune hemolytic anemia
  - Autoimmune mucocutaneous blistering disease (i.e., pemphigus vulgaris or pemphigus foliaceus)
  - The individual has had an inadequate response, contraindication, or intolerance to corticosteroids and the immune globulin will be used short term for this condition
  - Autoimmune neutropenia
  - Autoimmune uveitis
  - Chronic inflammatory demyelinating polyneuropathy
  - Dermatomyositis
  - The individual has had an inadequate response, contraindication, or intolerance to corticosteroids
  - Guillain-Barre syndrome
  - Idiopathic thrombocytopenia purpura
  - Multifocal motor neuropathy
  - Myasthenia gravis
  - Neonatal jaundice
  - Relapsing-remitting multiple sclerosis
  - von Willebrand disorder

- **Infectious and infection related diseases**
  - Cytomegalovirus (CMV) induced pneumonitis in solid organ transplants
  - Kawasaki’s disease
  - Respiratory syncytial virus
  - Sepsis
  - Toxic shock syndrome

- **Primary and secondary immunodeficiencies**
  - Chronic lymphocytic leukemia
  - Common variable immunodeficiency
  - Congenital X-linked agammaglobulinemia
- Hyperimmunoglobulinemia E. (hyper IgE) syndrome
- Hypogammaglobulinemia
- Multiple myeloma
- Other primary humoral immunodeficiency
- Pediatric human immunodeficiency virus
- Severe combined immunodeficiencies
- Wiskott-Aldrich syndrome
- Pre- and post transplant
  - Prophylaxis to reduce transplant rejection before transplant
  - Prophylaxis to reduce transplant rejection after transplant
  - Treatment of acute rejection

Approval duration: 180 days

**Safety Criteria**

- Thrombosis may occur with immune globulin products. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, the use of estrogens, indwelling vascular catheters, hyperviscosity and cardiovascular risk factors.
- Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur with the administration of immune globulin products in predisposed individuals. Renal dysfunction and acute renal failure occur more commonly in individuals receiving IVIG products containing sucrose.
- For individuals at risk of thrombosis, renal dysfunction, or renal failure, administer immune globulin at the minimum dose and infusion rate practicable. Ensure adequate hydration in individuals before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in individuals at risk for hyperviscosity.
- Contraindicated in IgA deficient individuals with antibodies to IgA and a history of hypersensitivity.
- For Gammaplex only: Contraindicated in individuals with hereditary intolerance to fructose, also in infants and neonates for whom sucrose or fructose tolerance has not been established.
- For Hizentra and Privigen only: Contraindicated in individuals with hyperprolinemia.

* Prescribers are alerted to the above safety concerns via educational points in the program.

**References**

16. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™) for Non-Hodgkin’s Lymphomas 2.2015. ©2015 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org.

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Lemtrada® (alemtuzumab) C9399, J3590

When requesting Lemtrada® (alemtuzumab), the individual requiring treatment must be diagnosed with an FDA-approved indication and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

**FDA-approved indication**

- Relapsing forms of multiple sclerosis

**Approved Off-label Compendial uses**

- No off-label uses meet evidence standards

**Coverage Guidelines**

### Multiple sclerosis (MS)

**Initial authorization:**
The individual meets all of the following criteria:¹

- Has a relapsing form of MS
- Does not have a human immunodeficiency virus (HIV) infection
- Had an inadequate response to 2 or more drugs indicated for treatment of MS (e.g., interferons, glatiramer acetate)

**Reauthorization:**
The individual meets all of the following criteria (2nd treatment course):

- Has a relapsing form of MS
- Does not have an HIV infection
- It has been 12 months since first Lemtrada® (alemtuzumab) treatment course
- Has not received 2 or more treatment courses of Lemtrada® (alemtuzumab)

**Additional Information for Prescribers**

- Lemtrada® (alemtuzumab) can cause the following: (Black Box Warning)*
  - Serious, sometime fatal, autoimmune conditions such as immune thrombocytopenia and anti-glomerular basement membrane disease
  - Serious and life-threatening infusion reactions
  - Increased risk of malignancies including thyroid cancer, melanoma, and lymphoproliferative disorders

*Because of the risk of autoimmune infusion reactions and malignancies, use of Lemtrada® (alemtuzumab) is monitored though a mandatory restricted distribution program, Lemtrada® (alemtuzumab) REMS program. This program requires that providers, patients, pharmacies and infusion facilities are enrolled and trained regarding
the ongoing monitoring requirements for an individual receiving/having received Lemtrada® (alemtuzumab).

- Lemtrada® (alemtuzumab) is contraindicated in an individual who is infected with HIV (contraindication)
- Pre-medication with high dose corticosteroids (1,000 mg methylprednisolone or equivalent) is recommended immediately prior to Lemtrada® (alemtuzumab) infusion and for the first 3 days of each treatment course
- The initiation of Lemtrada® (alemtuzumab) should be delayed in an individual with an active infection until the infection is fully controlled
- Live viral vaccines (e.g., FluMist®, oral polio vaccine [OPV], rotavirus, typhoid, yellow fever, measles, varicella, herpes zoster) should not be administered following a course of Lemtrada® (alemtuzumab)
- Complete blood counts with differential, serum creatinine levels and urinalysis with urine counts should be monitored at baseline and at periodic intervals for 48 months after the last dose; thyroid function tests should be done prior to treatment and every 3 months for 48 months after the last dose; skin should be examined at baseline and yearly for individuals receiving Lemtrada® (alemtuzumab)
- Administration of antiviral agent for herpetic prophylaxis is recommended starting on the first day of Lemtrada® (alemtuzumab) dosing and continuing for a minimum of 2 months after completion of Lemtrada® (alemtuzumab) dosing or until CD4+ count is more than 200 cells per microliter, whichever occurs later
- For individuals with a negative or unknown history of varicella or varicella zoster virus (VZV) vaccination, vaccination is recommended if antibody-negative

* Prescribers are alerted to this safety concern via educational points in the program.

References

Leukine® (sargramostim) Injection J2820

When requesting Leukine® (sargramostim), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications or approved off-label compendial requirements and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**

- Use following induction chemotherapy in acute myelogenous leukemia
- Use in mobilization and following transplantation of autologous peripheral blood progenitor cells
- Use in myeloid reconstitution after autologous bone marrow transplantation
- Use in myeloid reconstitution after allogeneic bone marrow transplantation
- Use in bone marrow transplantation failure or engraftment delay

**Approved Off-label Compendial uses**

- For prophylaxis of chemotherapy-induced febrile neutropenia
- For treatment of chemotherapy-induced febrile neutropenia
- Crohn’s disease
- To enhance hepatitis B vaccination response
- Metastatic melanoma
- For treatment of pulmonary alveolar proteinosis
- For metastatic renal cell carcinoma
- To promote wound healing
- Myelodysplastic syndrome

**Coverage Guidelines**

**For all indications:**
The individual does **not** have a known hypersensitivity to granulocyte-macrophage colony-stimulating factor (GM-CSF), yeast-derived products or any component of the product.

**For prophylaxis of chemotherapy-induced febrile neutropenia**

- The individual has a solid tumor or non-myeloid malignancy and
- The individual has experienced febrile neutropenia or dose-limiting neutropenic event with prior chemotherapy cycle or

The individual has one of the following risk categories for febrile neutropenia:

- For high risk for febrile neutropenia:
  - The intent of chemotherapy is curative/adjuvant or to prolong survival or
  - The intent of chemotherapy is symptom management. The risk of febrile neutropenia is not due to the chemotherapy regimen. If risk of febrile neutropenia is...
neutropenia is due to the chemotherapy regimen, the use of less myelosuppressive chemotherapy or dose reduction is not an option

- For intermediate risk for febrile neutropenia:
  - The intent of chemotherapy is curative/adjuvant or
  - The intent of chemotherapy is to prolong survival or to manage symptoms.
  - The risk of febrile neutropenia is not due to the chemotherapy regimen. If risk of febrile neutropenia is due to the chemotherapy regimen, the use of less myelosuppressive chemotherapy or dose reduction is not an option

- For low risk of febrile neutropenia:
  - The intent of chemotherapy is curative/adjuvant and
  - The individual is at significant risk for serious medical consequences of febrile neutropenia, including death

For treatment of chemotherapy-induced febrile neutropenia:

- The individual has a solid tumor or non-myeloid malignancy and
- The individual has received sargramostim as prophylaxis or has risk factors an infection-associated complications (i.e., sepsis syndrome, age >65 years, severe neutropenia [absolute neutrophil count <100/mcL], neutropenia expected to be more than 10 days in duration, pneumonia, invasive fungal infection, other clinically documented infections, hospitalization at the time of fever, prior episode of febrile neutropenia)

For myelodysplastic syndrome:

- The individual has recurrent infections or refractory cytopenia

For acute myeloid leukemia:

- The individual does not have excessive leukemic myeloid blasts in the bone marrow or peripheral blood (≥10%) and
- The individual is receiving induction chemotherapy

For autologous bone marrow transplantation:

- The individual has one of the following cancer diagnoses: non-Hodgkin’s lymphoma, Hodgkin’s disease, or acute lymphoblastic lymphoma

Additional Information for Prescribers

- Contraindicated in an individual with excessive leukemic myeloid blasts in the bone marrow or peripheral blood (≥10%)
- Contraindicated in an individual with known hypersensitivity to GM-CSF, yeast-derived products or any component of the product
- *Do not administer simultaneously with cytotoxic chemotherapy or radiotherapy or within 24 hours preceding or following chemotherapy or radiotherapy

* Prescribers are alerted to this safety concern via educational points in the program.
References


2. National Comprehensive Cancer Network Drugs & Biologics Compendium (NCCN Compendium®) Accessed November 13, 2015. [http://www.nccn.org/professionals/drug_compendium/content/contents.asp](http://www.nccn.org/professionals/drug_compendium/content/contents.asp) Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™). ©2015 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to [NCCN.org](http://www.nccn.org).


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Lucentis® (ranibizumab) injection J2278

When requesting Lucentis® (ranibizumab), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications or the approved off-label compendial use and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**

- Neovascular (wet) age-related macular degeneration (AMD)
- Macular edema following retinal vein occlusion (RVO)
- Diabetic macular edema (DME)
- Diabetic retinopathy (DR) in patients with DME

**Approved Off-label Compendial uses**

- Choroidal retinal neovascularization, secondary to pathologic myopia

**Coverage Guidelines**

For all approved indications the individual meets both of the following criteria for approval:
- Does not have ocular or periocular infection
- Does not have active intraocular inflammation

**Additional Information for Prescribers**

- None

**References**

Macugen® (pegaptanib) injection J2503

When requesting Macugen® (pegaptanib), the individual requiring treatment must be diagnosed with the following FDA-approved indication or the approved off-label compendial use and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**

- Neovascular (Wet) age-related macular degeneration (AMD)

**Approved Off-label Compendial uses**

- Diabetic macular edema (DME)

**Coverage Guidelines**

For all approved indications the individual meets the following criteria for approval:
- Does not have ocular or periocular infection

**Additional Information for Prescribers**

- None

**References**

Neulasta® (pegfilgrastim) Injection J2505

When requesting Neulasta® (pegfilgrastim), the individual requiring treatment must be diagnosed with FDA-approved or approved off-label compendial requirements and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

### FDA-approved indication

- To decrease the incidence of infection, as manifested by febrile neutropenia, in individuals with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia

### Approved Off-label Compendial uses

- For individuals undergoing mobilization of hematopoietic progenitor cells
- For individuals undergoing bone marrow transplantation

### Coverage Guidelines

**For all indications:**
The individual does NOT have a history of serious allergic reactions to filgrastim (Neupogen)

**For prophylaxis of chemotherapy-induced febrile neutropenia**
- The individual has a solid tumor or non-myeloid malignancy AND
- The individual has experienced febrile neutropenia or dose-limiting neutropenic event with prior chemotherapy cycle OR

Individual has one of the following risk categories for febrile neutropenia:
- For high risk for febrile neutropenia:
  - The intent of chemotherapy is curative/adjuvant or to prolong survival OR
  - The intent of chemotherapy is symptom management. The risk of febrile neutropenia is NOT due to the chemotherapy regimen. If risk of febrile neutropenia is due to the chemotherapy regimen, the use of less myelosuppressive chemotherapy or dose reduction is NOT an option
- For intermediate risk for febrile neutropenia:
  - The intent of chemotherapy is curative/adjuvant OR
  - The intent of chemotherapy is to prolong survival or to manage symptoms. The risk of febrile neutropenia is NOT due to the chemotherapy regimen. If risk of febrile neutropenia is due to the chemotherapy regimen, the use of less myelosuppressive chemotherapy or dose reduction is NOT an option
- For low risk of febrile neutropenia, the intent of chemotherapy is curative/adjuvant and individual is at significant risk for serious medical consequences of febrile neutropenia, including death
Safety Criteria

- Contraindicated to individuals with a history of serious allergic reactions filgrastim
- *Do not administer Neulasta between 14 days before and 24 hours after cytotoxic chemotherapy

* Prescribers are alerted to this safety concern via educational points in the program.

Approval duration: 180 days

References

Neupogen® (filgrastim) Injection J1442

When requesting Neupogen® (filgrastim), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications or approved off-label compendial requirements and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**

- To decrease the incidence of infection, as manifested by febrile neutropenia, in an individual with a non-myeloid malignancy receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever. 
- To reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment for an individual with acute myeloid leukemia. 
- To reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in an individual with a non-myeloid malignancy undergoing myeloablative chemotherapy followed by bone marrow transplantation. 
- To mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis. 
- To reduce the incidence and duration of sequelae of severe neutropenia in a symptomatic individual with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia. 
- To increase survival in an individual acutely exposed to myelosuppressive doses of radiation.

**Approved Off-label Compendial uses**

- For treatment of chemotherapy-induced febrile neutropenia. 
- To revere neutropenia caused by human immunodeficiency virus (HIV) infection. 
- For an individual undergoing esophagectomy. 
- Myelodysplastic syndrome. 
- For leukemia relapse after allogeneic stem cell transplantation. 

**Coverage Guidelines**

For all indications:
The individual does not have a history of a serious allergic reaction to pegfilgrastim.

For prophylaxis of chemotherapy-induced febrile neutropenia:
- The individual has a solid tumor or non-myeloid malignancy and 
- The individual has experienced febrile neutropenia or dose-limiting neutropenic event with prior chemotherapy cycle or 
- The individual has one of the following risk categories for febrile neutropenia: 
- For high risk for febrile neutropenia:
The intent of chemotherapy is curative/adjuvant or to prolong survival or the intent of chemotherapy is symptom management. The risk of febrile neutropenia is not due to the chemotherapy regimen. If risk of febrile neutropenia is due to the chemotherapy regimen, the use of less myelosuppressive chemotherapy or dose reduction is not an option.

For intermediate risk for febrile neutropenia:
- The intent of chemotherapy is curative/adjuvant or
- The intent of chemotherapy is to prolong survival or to manage symptoms. The risk of febrile neutropenia is not due to the chemotherapy regimen. If risk of febrile neutropenia is due to the chemotherapy regimen, the use of less myelosuppressive chemotherapy or dose reduction is not an option.

For low risk of febrile neutropenia:
- The intent of chemotherapy is curative/adjuvant and
- The individual is at significant risk for serious medical consequences of febrile neutropenia, including death.

For treatment of chemotherapy-induced febrile neutropenia:
- The individual has a solid tumor or non-myeloid malignancy and
- The individual has received filgrastim as prophylaxis or has risk factors for an infection associated complications (i.e. sepsis syndrome, age >65 years, severe neutropenia [absolute neutrophil count <100/mcL], neutropenia expected to be more than 10 days in duration, pneumonia, invasive fungal infection, other clinically documented infections, hospitalization at the time of fever, prior episode of febrile neutropenia).

For myelodysplastic syndrome:
- The individual has symptomatic anemia with low risk disease and
- The individual has serum erythropoietin level less than or equal to 500 mU/mL and Neupogen® (filgrastim) will be used in combination with epoetin alfa or darbepoetin alf.

For acute myeloid leukemia:
- The individual is receiving induction or consolidation chemotherapy.

Additional Information for Prescribers:
- Contraindicated in an individual with a history of a serious allergic reaction to pegfilgrastim
- *Do not administer Neupogen® (filgrastim) within 24 hours prior to or within 24 hours after completion of chemotherapy

*Prescribers are alerted to this safety concern via educational points in the program.
References

3. National Comprehensive Cancer Network Drugs & Biologics Compendium (NCCN Compendium®) Accessed November 13, 2015. [http://www.nccn.org/professionals/drug_compendium/content/contents.asp](http://www.nccn.org/professionals/drug_compendium/content/contents.asp) Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™). ©2015 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to [NCCN.org](http://www.nccn.org).
Opdivo® (nivolumab) J9299

When requesting Opdivo® (nivolumab), the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

FDA-approved indications

Melanoma
- As a single agent for the treatment of an individual with BRAF V600 wild-type unresectable or metastatic melanoma.¹
- As a single agent for the treatment of an individual with unresectable or metastatic, BRAF V600 mutation-positive melanoma and disease progression following ipilimumab and a BRAF inhibitor.¹
- In combination with ipilimumab, for the treatment of an individual with BRAF V600 wild-type, unresectable or metastatic melanoma.¹

Non-Small Cell Lung Cancer
- For the treatment of an individual with metastatic non-small cell lung cancer with progression on or after platinum-based chemotherapy. An individual with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Opdivo (nivolumab).¹

Renal Cell Carcinoma
- For the treatment of an individual with advanced renal cell carcinoma who have received prior anti-angiogenic therapy.¹

Approved Off-label Compendial uses

Melanoma
- Therapy for metastatic or unresectable disease as a single agent or in combination with ipilimumab as:
  - first-line therapy
  - second-line or subsequent therapy for disease progression for individuals with performance status of 0-2 if not previously used.²

Non-Small Cell Lung Cancer
- Preferred single agent (if not already given) as subsequent therapy for metastatic disease in individuals with performance status of 0-2 following progression on a first-line cytotoxic regimen or for further progression on other systemic therapy.²
Renal Cell Carcinoma
- Subsequent therapy as single agent for relapse or surgically unresectable stage IV disease with predominant clear cell histology that progressed on prior tyrosine kinase inhibitor therapy.2

Coverage Guidelines

Melanoma
- The individual has unresectable or metastatic disease.2
- If Opdivo (nivolumab) was previously used, the individual did not experience disease progression while on Opdivo (nivolumab).2
- Opdivo (nivolumab) is being used as a single agent or in combination with Yervoy (ipilimumab).2
- Opdivo (nivolumab) will be used as either:
  - First-line or
  - Second-line or subsequent therapy with performance status of 0-2.2

Non-Small Cell Lung Cancer
- The individual has metastatic disease.2
- If Opdivo (nivolumab) was previously used, the individual did not experience disease progression while on Opdivo (nivolumab).2
- Opdivo (nivolumab) is being used as a single agent for subsequent therapy.2
- The individual has experienced disease progression on a first-line cytotoxic regimen or other systemic therapy.2
- The individual's performance status is 0-2.2

Renal Cell Carcinoma
- The individual has relapsed or unresectable stage IV disease.2
- The histology is predominant clear cell.2
- Opdivo (nivolumab) is being used as a single agent for subsequent therapy.2
- The individual has experienced disease progression on prior tyrosine kinase inhibitor therapy.2

The approval duration is for 12 months.

Additional Information for Prescribers

Dosage and Administration
- Opdivo (nivolumab) is administered as an intravenous infusion over 60 minutes.1
- For unresectable or metastatic melanoma1:
  - Opdivo (nivolumab) 3 mg/kg every 2 weeks.1
  - Opdivo (nivolumab) in combination with Yervoy (ipilimumab): Opdivo (nivolumab) 1 mg/kg, followed by Yervoy (ipilimumab) on the same day, every 3 weeks for 4 doses, then Opdivo (nivolumab) 3 mg/kg every 2 weeks.1
• For metastatic non-small cell lung cancer1:
  ▪ Opdivo (nivolumab) 3 mg/kg every 2 weeks.1
• For advanced renal cell carcinoma1:
  ▪ Opdivo (nivolumab) 3 mg/kg every 2 weeks.1

References

Orencia® (abatacept) Injection J0129

When requesting Orencia® (abatacept), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-approved indications

Rheumatoid Arthritis (RA)
- An adult with moderately- to severely-active rheumatoid arthritis. Orencia® may be used as monotherapy or concomitantly with disease-modifying antirheumatic drugs (DMARDs) other than tumor necrosis factor (TNF) antagonists.

Polyarticular Juvenile Idiopathic Arthritis (PJIA)
- An individual 6 years of age and older with moderately- to severely-active polyarticular juvenile idiopathic arthritis. Orencia® may be used as monotherapy or concomitantly with methotrexate.

Approved Off-label Compendial uses

- No off-label uses meet evidence standards

Coverage Guidelines

For all indications:
- The individual does not have an active infection (including active tuberculosis or any clinically important localized infection)¹
- Orencia® (abatacept) will not be used in combination with another biologic agent¹
- For Orencia® (abatacept) reauthorization request, the individual’s condition must have improved or stabilized with at least 6 months of therapy³
- For Orencia® (abatacept) initial authorization, the individual has been screened for latent TB.¹ For positive latent TB, the individual must have started/completed or will be treated for TB prior to starting Orencia® (abatacept) ¹

Rheumatoid Arthritis (initial authorization):
The individual meets one of the following for approval:
- Had an inadequate response or intolerance to prior biologic agent or
- The disease is moderately- to severely-active and had an inadequate response or intolerance (including contraindication) to at least one non-biologic DMARD³,⁴ or
- Has poor prognostic features (i.e. functional limitation, extraarticular disease, positive rheumatoid factor or anti-cyclic citrullinated peptide antibodies, or bony erosions by radiograph)³ and had an inadequate response or intolerance (including contraindication) to at least one non-biologic DMARD³,⁴
Polyarticular Juvenile Idiopathic Arthritis (initial authorization):
The individual meets one of the following for approval:
• Had an inadequate response or intolerance to prior biologic agent or
• Had an inadequate response or intolerance (including contraindication) to at least one non-biologic DMARD

Additional Information for Prescribers¹

• Must perform test for latent TB infection; if positive, must start treatment for TB prior to starting Orencia®(abatacept)
• The individual must be monitored for active TB during treatment, even if initial latent TB test is negative*
• Concomitant use with a TNF antagonist can increase the risk of infections and serious infections. Orencia® (abatacept) must be discontinued if a serious infection develops
• *Avoid use of live vaccines (e.g., FluMist®, oral polio vaccine [OPV], rotavirus, typhoid, yellow fever, measles, varicella, herpes zoster) concurrently or within 3 months of discontinuation of Orencia® (abatacept)

* Prescribers are alerted to this safety concern via educational points in the program.

References
Prolia® (denosumab) J0897

When requesting Prolia® (denosumab), the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

FDA-approved indications

- Treatment of osteoporosis in postmenopausal women
- Treatment of osteoporosis in men
- Treatment of bone loss in men with prostate cancer
- Treatment of bone loss in women with breast cancer

Approved Off-label Compendial uses

- Prophylaxis of osteoporosis in postmenopausal women
- Prevention of bone loss in men with prostate cancer

Coverage Guidelines

Treatment of osteoporosis in postmenopausal women

- The patient is at high risk for fracture, defined as:
  - History of an osteoporotic fracture
  - Multiple risk factors for fracture**2,3,5 AND a baseline bone mineral density (BMD) T-score by DXA (dual-energy x-ray absorptiometry) of ≤ -2.51
  - FRAX® 10-year fracture probability of ≥ 20% or hip fracture probability of ≥ 3% 8 AND a baseline bone mineral density (BMD) T-score by DXA of ≤ -2.51
  - OR the patient has had an inadequate response, intolerance, or contraindication to other available osteoporosis therapies such as bisphosphonates plus a baseline bone mineral density (BMD) T-score by DXA of ≤ -2.51

Prophylaxis of osteoporosis in postmenopausal women

- The patient meets one of the following criteria for approval:
  - Patient has multiple risk factors for fracture**2,3,5 AND a baseline bone mineral density (BMD) T-score by DXA between -1 and -2.52,3,6
  - FRAX® 10-year fracture probability of ≥ 20% or hip fracture probability of ≥ 3%8 AND a baseline bone mineral density (BMD) T-score by DXA between -1 and -2.52,3,6

Treatment of osteoporosis in men

- The patient is at high risk for fracture, defined as:
  - History of an osteoporotic fracture
  - Multiple risk factors for fracture**2,4,5 AND a baseline bone mineral density (BMD) T-score by DXA of ≤ -21,6
• FRAX® 10-year fracture probability of ≥ 20% or hip fracture probability of ≥ 3% AND a baseline bone mineral density (BMD) T-score by DXA of ≤ -21,6
• OR the patient has had an inadequate response, intolerance, or contraindication to other available osteoporosis therapies such as bisphosphonates AND a baseline bone mineral density (BMD) T-score by DXA of ≤ -21,6

Prevention or treatment of bone loss in men with prostate cancer
• The patient is at high risk for fracture, defined as:
  ▪ History of an osteoporotic fracture
  ▪ Multiple risk factors for fracture**5 AND a baseline bone mineral density (BMD) T-score by DXA of -1 or less1,6
  ▪ FRAX® 10-year fracture probability of ≥ 20% or hip fracture probability of ≥ 3%8 AND a baseline bone mineral density (BMD) T-score by DXA of -1 or less1,6
• The patient is receiving androgen deprivation therapy

Treatment of bone loss in women with breast cancer
• The patient is at high risk for fracture, defined as:
  ▪ History of an osteoporotic fracture
  ▪ Multiple risk factors for fracture**5 AND a baseline bone mineral density (BMD) T-score by DXA of -1 or less1,6
  ▪ FRAX® 10-year fracture probability of ≥ 20% or hip fracture probability of ≥ 3%8 AND a baseline bone mineral density (BMD) T-score by DXA of -1 or less1,6
• The patient is receiving aromatase inhibitor therapy

Safety Criteria (for all approved indications)
• If the patient is of childbearing potential, pregnancy has been ruled out.
• The patient does not have hypocalcemia (defined as serum calcium or corrected calcium* less than 8.5 mg/dL).
• The following safety concerns are alerted to our prescribers as educational points/reminders:
  ▪ Osteonecrosis of the jaw can occur in patients receiving Prolia. A routine oral examination should be performed prior to starting Prolia. Symptoms should be monitored. Clinical judgment of the treating physician and/or oral surgeon should guide the management of patients requiring invasive dental procedures.
  ▪ Atypical femoral fracture has been reported with Prolia. Patients with thigh or groin pain should be evaluated to rule out a femoral fracture.
  ▪ All patients with severe renal impairment (defined as patients on dialysis or with a CrCl < 30 mL/min) should be instructed about the importance of maintaining calcium levels with adequate calcium and vitamin D supplementation.
  ▪ In patients predisposed to hypocalcemia and disturbances of mineral metabolism (e.g. history of hypoparathyroidism, thyroid surgery, parathyroid surgery, malabsorption syndromes, excision of small intestine, severe renal
impairment [creatinine clearance < 30 mL/min] or receiving dialysis), clinical monitoring of calcium and mineral levels (phosphorus and magnesium) is highly recommended within 14 days of Prolia injection.

*Corrected calcium (XX.X mg/dL) = measured serum calcium (XX.0 mg/dL) + 0.8 (4.0 - serum albumin [XX.X g/dL]) where 4.0 represents the average albumin level in g/dL.

** A prior fragility fracture, parental history of hip fracture, current tobacco smoking, secondary causes of osteoporosis (e.g., rheumatoid arthritis, hypogonadism, use of phenytoin, phenobarbital, long term warfarin, etc.), daily alcohol use of three or more drinks per day, advanced age (greater than 65), body habitus (weight less than 127 lbs or BMI less than or equal to 20), Caucasian or Asian race, sedentary lifestyle, diet deficient in calcium or vitamin D without adequate supplementation, long-term use of corticosteroids (defined as greater than 3 continuous months), early menopause, etc. (Please note: this list is not all-inclusive)

The approval duration is for 12 months.

Additional Information for Prescribers

- None

References

Provenge® (sipuleucel-T) Q2043

When requesting Provenge® (sipuleucel-T), the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**¹

- Provenge (sipuleucel-T) is an autologous cellular immunotherapy indicated for the
treatment of asymptomatic or minimally symptomatic metastatic castrate-resistant (hormone-refractory) prostate cancer

**Approved Off-label Compendial uses**

- None

**Coverage Guidelines**

**Prostate Cancer**

Patient meets ALL of the following criteria:¹,²

- Has castration- recurrent metastatic disease
- Is asymptomatic or minimally symptomatic
- Has performance status 0-1
- Has life expectancy of greater than 6 months
- Has no hepatic metastases
- Does not exceed 3 doses of sipuleucel-T

**Additional Information for Prescribers**¹

- The recommended course of therapy for Provenge is 3 complete doses, given at approximately 2-week intervals.
- Acute infusion reactions may occur. If reactions occur, rate of infusion must be decreased or stopped and appropriate medical treatment must be administered
- Syncope and hypotension have been observed. Patient with cardiac or pulmonary conditions should be monitored closely
- Provenge should be used with caution in patient with risk factors for thromboembolic events
References


Reclast® and Zometa® (zoledronic acid) Injection J3487, J3488, J3489, Q2051

When requesting Reclast® (zoledronic acid) or Zometa® (zoledronic acid), the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**

**Reclast® (zoledronic acid)**
- Treatment of osteoporosis in a postmenopausal woman or for osteoporosis in a man
- Prevention of osteoporosis in a postmenopausal woman
- Glucocorticoid-induced osteoporosis
- Paget’s disease of bone

**Zometa® (zoledronic acid)**
- Hypercalcemia of malignancy
- Multiple myeloma
- Bone metastases from solid tumors

**Approved Off-label Compendial uses**

**Zometa® (zoledronic acid)**
- Monoclonal gammopathy of uncertain significance with osteopenia or osteoporosis
- Prevention or treatment of osteoporosis during androgen deprivation therapy
- Osteopenia, secondary to hormone therapy in breast cancer patients
- Osteopenia, secondary to ovarian dysfunction induced by adjuvant chemotherapy in a premenopausal woman with early-stage breast cancer

**Coverage Guidelines**

**Reclast® (zoledronic acid)**
- Treatment of osteoporosis in a postmenopausal woman or for osteoporosis in a man:
  - The patient meets at least one of the following criteria for approval:
    - The patient has a bone mineral density (BMD) T-score of ≤ -2.5 by dual-energy x-ray absorptiometry (DXA)
    - The patient has a history of osteoporotic fractures
  - Reclast (zoledronic acid) dosing: 5 mg once a year
- Prevention of osteoporosis in a postmenopausal woman:
  - The patient has a BMD T-score of -1 to -2.5 by DXA
- The patient has had an inadequate response, contraindication or intolerance to an oral bisphosphonate agent (e.g., alendronate, risedronate, etc.)†
- Reclast (zoledronic acid) dosing: 5 mg once every 2 years1

- Glucocorticoid-induced osteoporosis1:
  - The patient is a postmenopausal woman or man ≥ 50 years of age5:
    - With a high fracture‡ risk5
      - The patient has had an inadequate response, contraindication or intolerance to an oral bisphosphonate agent (e.g., alendronate, risedronate, etc.)†
      - Reclast (zoledronic acid) dosing: 5 mg once a year1
    - With a medium to low fracture‡ risk5
      - The patient’s glucocorticoid dose is ≥ 7.5 mg/day of prednisone or its equivalent5
      - The patient has had an inadequate response, contraindication or intolerance to an oral bisphosphonate agent (e.g., alendronate, risedronate, etc.)†.
      - Reclast (zoledronic acid) dosing: 5 mg once a year1
  - The patient is a premenopausal woman of non-childbearing potential or a man < 50 years of age5
    - The patient has a history of a fragility fracture§5
      - The anticipated duration of the glucocorticoid therapy is > 3 months5
        - The patient has had an inadequate response, contraindication or intolerance to an oral bisphosphonate agent (e.g., alendronate, risedronate, etc.)†
        - The anticipated duration of the glucocorticoid therapy is 1-3 months5
          - The patient’s glucocorticoid dose is ≥ 7.5 mg/day of prednisone or its equivalent5
          - Reclast (zoledronic acid) dosing: 5 mg once a year1

- Paget’s disease of bone1:
  - The patient meets at least one of the following criteria for approval1:
    - The patient has elevations of serum alkaline phosphatase of ≥ 2x ULN1
    - The patient is symptomatic1
    - The patient is at risk for disease complications1
  - For initial treatment1
    - Reclast (zoledronic acid) dosing: a single 5mg infusion1
  - For retreatment1
    - The patient meets at least one of the following criteria for retreatment1:
      - The patient has relapsed based on increases in serum alkaline phosphatase1
The patient has failed to achieve normalization of serum alkaline phosphatase\(^1\)
- The patient is symptomatic\(^1\)
  - Reclast (zoledronic acid) dosing: a single 5mg infusion\(^1\)

**Reclast® (zoledronic acid) - For all indications**
- The patient does not have any of the following contraindications or exclusions to therapy\(^1\):
  - Hypocalcemia (defined as an albumin-corrected calcium* < 8.5 mg/dL)\(^1\)
  - Creatinine clearance < 35 mL/min\(^1\)
  - Evidence of acute renal impairment\(^1\)

\(^*\)Albumin-corrected Ca in mg/dL = Ca in mg/dL + 0.8 (4.0 g/dL - patient albumin [g/dL])

\(^\dagger\)This is an optional step therapy/point of management for clients looking to put stricter criteria requirements in place to help manage drug spend. This step therapy is not spelled out in national guidelines. (Of note: costs of Reclast [zoledronic acid] need to be compared to oral bisphosphonates.)

\(^\ddagger\)For more information on fracture risk categories, refer to American College of Rheumatology (ACR) 2010 guidelines for glucocorticoid-induced osteoporosis (Figure 2 and/or FRAX score) available at:

\(^\S\)A fracture caused by injury that would be insufficient to fracture normal bone.

**Zometa® (zoledronic acid)**
- Hypercalcemia of malignancy\(^6\)
  - The patient’s albumin-corrected calcium* is ≥ 12 mg/dL\(^6\)
  - For initial treatment:\(^6\)
    - Zometa (zoledronic acid) dosing: a single 4 mg infusion\(^6\)
  - For retreatment:\(^6\)
    - The patient’s serum calcium level has not returned to normal or does not remain normal after initial treatment\(^6\)
    - Zometa (zoledronic acid) will be given ≥ 7 days after the initial dose\(^6\)
    - Zometa (zoledronic acid) dosing: a single 4 mg infusion\(^6\)

- Multiple myeloma\(^6\)
  - Zometa (zoledronic acid) will be used in conjunction with standard antineoplastic therapy\(^6\)
  - Zometa (zoledronic acid) dosing: up to 4 mg (depending on CrCl) every 3 to 4 weeks\(^6\)

- Bone metastases from solid tumors
  - The patient’s primary cancer diagnosis is prostate cancer\(^8\)
    - The patient has castration-recurrent prostate cancer\(^8\)
Zometa (zoledronic acid) will be used in conjunction with standard antineoplastic therapy.

- Zometa (zoledronic acid) dosing: up to 4 mg (depending on CrCl) every 3 to 4 weeks.

The patient’s primary cancer diagnosis is something other than prostate cancer.

- Zometa (zoledronic acid) will be used in conjunction with standard antineoplastic therapy.
- Zometa (zoledronic acid) dosing: up to 4 mg (depending on CrCl) every 3 to 4 weeks.

- Monoclonal gammopathy of uncertain significance with osteopenia or osteoporosis.
  - Zometa (zoledronic acid) dosing: 4 mg every 6 months.

- Prevention or treatment of osteoporosis during androgen deprivation therapy.
  - The patient is at high risk for fractures.
  - Zometa (zoledronic acid) dosing: 4 mg every 3 months.

- Osteopenia, secondary to hormone therapy in breast cancer patients.
  - Zometa (zoledronic acid) dosing: 4 mg every 6 months.

- Osteopenia, secondary to ovarian dysfunction induced by adjuvant chemotherapy in a premenopausal woman with early-stage breast cancer.
  - Zometa (zoledronic acid) dosing: 4 mg every 3 to 6 months.

*Albumin-corrected Ca in mg/dL = Ca in mg/dL + 0.8 (4.0 g/dL - patient albumin [g/dL]).

*A patient’s fracture risk can be assessed using FRAX®. ADT should be considered “secondary osteoporosis” using the FRAX® algorithm.

### Additional Information for Prescribers

- None

### References


Remicade® (infliximab) J1745

When requesting Remicade (infliximab), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications or compendial approved uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**

Remicade® (infliximab) is indicated for the following FDA-approved uses:

- For reducing signs and symptoms and inducing and maintaining clinical remission in an adult with moderately- to severely-active Crohn’s disease who has had an inadequate response to conventional therapy. Remicade® (infliximab) is indicated for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in an adult with fistulizing Crohn’s disease.
- For reducing signs and symptoms and inducing and maintaining clinical remission in a pediatric individual 6 years of age and older with moderately- to severely-active Crohn’s disease who has had an inadequate response to conventional therapy.
- For reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in an adult with moderately- to severely-active ulcerative colitis who has had an inadequate response to conventional therapy.
- For reducing signs and symptoms and inducing and maintaining clinical remission in a pediatric individual 6 years of age and older with moderately- to severely-active ulcerative colitis who has had an inadequate response to conventional therapy.
- In combination with methotrexate, is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in an individual with moderately- to severely-active rheumatoid arthritis.
- For reducing signs and symptoms in an individual with active ankylosing spondylitis.
- For reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in an individual with psoriatic arthritis.
- For the treatment of an adult with chronic severe (i.e., extensive and/or disabling) plaque psoriasis who is a candidate for systemic therapy and when other systemic therapies are medically less appropriate.

**Approved Off-label Compendial uses**

Remicade® (infliximab) is indicated for the following compendial uses:

- Adult-onset Still’s disease
- Severe, refractory hidradenitis suppurativa
- Polyarticular juvenile idiopathic arthritis, refractory to nonbiologic DMARDs
- Synovitis
- Refractory Takayasu’s disease
- Refractory uveitis
• Refractory Wegener’s granulomatosis in combination with corticosteroids

**Coverage Guidelines**

The individual has one of the following diagnoses and meets the following criteria for coverage:

**Initial authorization for Remicade® (infliximab) therapy :**

- **Rheumatoid arthritis (RA)**¹
  - The individual meets the following criteria for approval:
    - Remicade® (infliximab) will be taken in combination with methotrexate¹,² and
    - Has had an inadequate response or intolerance to a prior biologic agent²,⁹ or
    - Has moderately- to severely-active rheumatoid arthritis¹ and has tried and had an inadequate response, intolerance or contraindication to at least one non-biologic disease modifying antirheumatic drug (DMARD)²,⁹
    - or
    - Has poor prognostic factors such as functional limitation, extraarticular disease, positive rheumatoid factor or anti-cyclic citrullinated peptide antibodies, or bony erosions by radiograph²,⁹
    - and
    - Has tried and had an inadequate response, intolerance or contraindication to at least one non-biologic disease modifying antirheumatic drug (DMARD)²,⁹

- **Moderately-to severely-active psoriatic arthritis**⁵,¹⁰

- **Active ankylosing spondylitis**¹
  - The individual has had an inadequate response, intolerance, or contraindication to non-steroidal anti-inflammatory drugs (NSAIDs)⁴

- **Chronic, severe plaque psoriasis**¹
  - The individual has had an inadequate response, intolerance, or contraindication to either phototherapy or oral conventional systemic therapy (e.g., methotrexate, cyclosporine, acitretin)¹,¹¹

- **Crohn’s disease**¹
  - The individual has fistulizing Crohn’s disease or
  - The individual has moderately- to severely-active disease
  - The individual has had an inadequate response, intolerance, or contraindication to conventional therapy (e.g., corticosteroids, sulfasalazine, azathioprine, 6-mercaptopurine, etc.)¹,⁶,⁷

- **Ulcerative colitis**¹
  - The individual has moderately- to severely-active disease
  - The individual has had an inadequate response, intolerance, or contraindication to conventional therapy (e.g., corticosteroids, sulfasalazine, azathioprine, 6-metcaptapurine, etc.)¹,⁸
The prescribed drug is being requested for one of the following compendial uses\(^3\):
- Adult-onset Still’s disease
- Severe, refractory hidradenitis suppurativa
- Polyarticular juvenile idiopathic arthritis (JIA), refractory to nonbiologic DMARDs\(^*\)
- Synovitis
- Refractory Takayasu’s disease
- Refractory uveitis
- Refractory Wegener’s granulomatosis in combination with corticosteroids

For all indications, the individual meets all of the following safety criteria for approval:
- Either does not have moderate to severe heart failure, NYHA Class III or IV, or if he/she does, then the prescribed dose does not exceed 5 mg/kg\(^1\)
- Does not have an active infection (including active tuberculosis or any clinically important localized infection)\(^1\)
- Remicade\(^\circledast\) (infliximab) will not be used in combination with another biologic agent\(^1\)
- Has been screened for latent TB infection\(^1\)
- Is negative for latent TB infection. Or if positive, has started or will be treated for latent TB prior to starting Remicade\(^\circledast\) (infliximab)\(^1\)
- Has been tested for hepatitis B virus (HBV) and if appropriate, HBV infection has been ruled out or treatment initiated\(^1\)

Reauthorization request for Remicade\(^\circledast\) (infliximab) therapy and the prescribed indication is one of the following is one of the following\(^1,3\):
- RA
- Active psoriatic arthritis
- Active ankylosing spondylitis
- Plaque psoriasis
- Crohn’s disease
- Ulcerative colitis
- Adult-onset Still’s disease
- Severe, refractory hidradenitis suppurativa
- Polyarticular juvenile idiopathic arthritis (JIA), refractory to nonbiologic DMARDs\(^*\)
- Synovitis
- Refractory Takayasu’s disease
- Refractory uveitis
- Refractory Wegener’s granulomatosis in combination with corticosteroids

and meets the following criteria for approval:
A. The individual’s condition has improved or stabilized with Remicade\(^\circledast\) (infliximab) therapy (after being on therapy for at least 6 months)
B. For all indications, the individual meets all of the following safety criteria for approval:
   1. Either does not have moderate to severe heart failure, NYHA Class III or IV, or if he/she does, then the prescribed dose will not exceed 5 mg/kg\(^1\)
2. Does not have an active infection (including active tuberculosis or any clinically important localized infection) \(^1\)

3. Remicade® (infliximab) will not be used with another biologic agent \(^1\)

*Methotrexate, Hydroxychloroquine, Sulfasalazine, etc.

**Additional Information for Prescribers**

An individual treated with Remicade® (infliximab) is at increased risk for developing serious infections that may lead to hospitalization or death (Black Box Warning). Most individuals who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. Remicade® (infliximab) should be discontinued if an individual develops a serious infection or sepsis. Reported infections include:

- Active tuberculosis, including reactivation of latent tuberculosis. Individuals with tuberculosis have frequently presented with disseminated or extrapulmonary disease. The individual should be tested for latent tuberculosis before Remicade® (infliximab) use and during therapy. Treatment for latent infection should be initiated prior to Remicade® (infliximab) use.
- Invasive fungal infections including histoplasmosis, coccidiodomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. An individual with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some individuals with active infection. Empiric anti-fungal therapy should be considered in an individual at risk for invasive fungal infections who develops severe systemic illness.
- Bacterial, viral and other infections due to opportunistic pathogens, including Legionella and Listeria.

The risks and benefits of treatment with Remicade® (infliximab) should be carefully considered prior to initiating therapy in an individual with chronic or recurrent infection.

Remicade® (infliximab) at doses >5 mg/kg should not be administered to an individual with moderate to severe heart failure. In a randomized study evaluating Remicade® (infliximab) in patients with moderate to severe heart failure (New York Heart Association [NYHA] Functional Class III/IV), Remicade® (infliximab) treatment at 10 mg/kg was associated with an increased incidence of death and hospitalization due to worsening heart failure. (Contraindications)

The following are some important safety concerns regarding the use of Remicade® (infliximab). The prescriber is alerted to these safety concerns via educational points in the program.

- The individual should be monitored for active tuberculosis (TB) during treatment, even if initial latent TB test is negative.
Hepatitis B virus (HBV) carriers should be monitored during and for several months after therapy. If reactivation occurs, Remicade® (infliximab) should be stopped and anti-viral therapy began.

It is recommended that live vaccines (e.g., FluMist®, oral polio vaccine [OPV], rotavirus, typhoid, yellow fever, measles, varicella, herpes zoster) not be given concurrently with Remicade® (infliximab). In addition, therapeutic infectious agents such as live attenuated bacteria should not be given concurrently with Remicade® (infliximab).

Fatal outcome due to disseminated BCG infection has been reported in an infant who received a BCG vaccine after in utero exposure to infliximab. At least a 6-month waiting period following birth is recommended before the administration of any live vaccine to infants exposed in utero to infliximab.

It is recommended that all pediatric individuals be brought up to date with all vaccinations prior to initiating Remicade® (infliximab) therapy.

For patients with Crohn’s disease/ulcerative colitis: the use of azathioprine or 6-mercaptopurine in combination with Remicade® (infliximab) may increase the risk of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma.

References

Rituxan® (rituximab) Injection J9310

When requesting Rituxan® (rituximab), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications or approved off-label compendial requirements and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-approved indications

Non Hodgkin’s Lymphoma (NHL)
Rituxan® (rituximab) is indicated for the treatment of an individual with any of the following:
- Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent
- Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in individuals achieving a complete or partial response to Rituxan® (rituximab) in combination with chemotherapy, as single-agent maintenance therapy
- Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line CVP chemotherapy
- Previously untreated diffuse large B-cell, CD20-positive NHL in combination with CHOP or other anthracycline-based chemotherapy regimens

Chronic Lymphocytic Leukemia (CLL)
Rituxan® (rituximab) is indicated, in combination with fludarabine and cyclophosphamide (FC), for the treatment of an individual with previously untreated and previously treated CD20-positive CLL.

Rheumatoid Arthritis (RA)
Rituxan® (rituximab) in combination with methotrexate is indicated for the treatment of an adult with moderately-to severely-active rheumatoid arthritis who has had an inadequate response to one or more TNF antagonist therapies

Granulomatosis with Polyangiitis (GPA) (Wegener’s Granulomatosis) and Microscopic Polyangiitis (MPA)
Rituxan® (rituximab) in combination with glucocorticoids is indicated for the treatment of an adult with granulomatosis with polyangiitis (GPA) (Wegener’s granulomatosis) and microscopic polyangiitis (MPA).

Approved Off-label Compendial uses

- Acute lymphoblastic leukemia
- Leptomeningeal metastases from lymphoma
- Primary central nervous system lymphoma
- Lymphocyte-predominant Hodgkin’s Lymphoma
• Non-Hodgkin's lymphoma (NHL)
• Waldenström macroglobulinemia/lymphoplasmacytic lymphoma
• Autoimmune hemolytic anemia
• Evans syndrome
• Graft versus Host disease unspecified
• Idiopathic Thrombocytopenia Purpura
• Minimal change disease (Nephritic syndrome)
• Pemphigus vulgaris, severe limited to severe disease
• Primary Sjögren’s syndrome
• Relapsing remitting multiple sclerosis
• Systemic lupus erythematosus
• Thrombotic thrombocytopenic purpura

**Coverage Guidelines**

For all indications, meet both of the following:
- The individual does not have severe, active infection and
- Prior to initiating Rituxan® (rituximab), individual has been screened for HBV infection
- For all oncology indications, patient must have CD20+ disease

**Rheumatoid Arthritis**

*Initial authorization*

The individual meets one of the following for approval:
- Had an inadequate response or intolerance to prior biologic agent and Rituxan® (Rituximab) will be used in combination with methotrexate or
- The disease is moderately- to severely-active and had an inadequate response or intolerance (including contraindication) to at least one non-biologic DMARD and Rituxan® (rituximab) will be used in combination with methotrexate or
- Has poor prognostic features (i.e. functional limitation, extraarticular disease, positive rheumatoid factor or anti-cyclic citrullinated peptide antibodies, or bony erosions by radiograph) and had an inadequate response or intolerance (including contraindication) to at least one non-biologic DMARD and Rituxan® (rituximab) will be used in combination with methotrexate

*Reauthorization*

The individual meets both of the following for approval:
- Rituxan® (rituximab) will be used in combination with methotrexate and
- The individual's condition has improved or stabilized with Rituxan® (rituximab) therapy and at least 16 weeks has elapsed since last infusion

**Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA)**
- Rituxan® (Rituximab) is used in combination with glucocorticoids
Graft versus Host disease or minimal change disease (nephritic syndrome)
- The individual’s disease is refractory to steroids

Thrombotic thrombocytopenia purpura
- Rituxan® (Rituximab) is used in combination with steroids and plasma exchange

Acute lymphoblastic leukemia
- The individual has CD20+ disease and
- The disease is Philadelphia chromosome-negative

Primary central nervous system lymphoma
- The individual has CD20+ disease and
- If requesting Rituxan® (rituximab) as primary treatment, individual has Karnofsky Performance Status (KPS) greater than or equal to 40 or
- The individual has progressive or recurrent disease

Hodgkin’s Lymphoma
- The individual has CD20+ disease and
- Has lymphocyte-predominant Hodgkin lymphoma subtype

Leptomeningeal metastases from lymphoma
- The individual has CD20+ disease

Waldenström’s macroglobulinemia/lymphoplasmacytic lymphoma
- The individual has CD20+ disease and
- The intent of therapy is to use Rituxan® (Rituximab) as primary therapy or
- For relapsed disease, the individual must have used Rituxan® (Rituximab) as a primary therapy

Non-Hodgkin’s lymphoma
- The individual has CD20+ disease and
- Must have one of the following subtypes:
  - AIDS-related B-cell lymphoma (Burkitt lymphoma, diffuse large B-cell lymphoma, primary effusion lymphoma or lymphoma associated with Castleman’s disease)
  - Burkitt’s lymphoma
  - Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma
  - Diffuse large B-cell lymphoma
  - Follicular lymphoma
  - Gastric MALT lymphoma
  - Relapsed or refractory hairy cell leukemia
  - Lymphoblastic lymphoma
  - Mantle cell lymphoma
  - Non-gastric MALT lymphoma
  - Post-transplant lymphoproliferative disorder
  - Primary cutaneous B-cell lymphoma
Splenic marginal zone lymphoma

Additional Information for Prescribers

- Fatal infusion reactions within 24 hours of Rituxan® (rituximab) have occurred. The individual must be monitored and Rituxan® (rituximab) infusion discontinued for severe reactions (Black Box Warning)
- *Severe, including fatal, mucocutaneous reactions can occur in an individual receiving Rituxan® (rituximab) (Black Box Warning)
- *Hepatitis B Virus (HBV) reactivation can occur in an individual treated with Rituxan® (rituximab), in some cases resulting in fulminant hepatitis, hepatic failure, and death. The individual must be screened for HBV infection before treatment initiation, and be monitored during and after treatment with Rituxan® (rituximab) (Black Box Warning)
- *Progressive Multifocal Leukoencephalopathy (PML), including fatal PML, can occur in an individual receiving Rituxan® (rituximab) (Black Box Warning)
- Rituxan® (rituximab) is not recommend for use in an individual with severe, active infections
- *Do not administer live virus vaccines (e.g., FluMist®, oral polio vaccine [OPV], rotavirus, typhoid, yellow fever, measles, varicella, herpes zoster) prior to or during Rituxan® (rituximab)

*Prescribers are alerted to this safety concern via educational points in the program.

References

Tysabri® (natalizumab) injection J2323

When requesting Tysabri® (natalizumab), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

### FDA-approved indications

- Multiple Sclerosis
- Crohn’s disease

### Approved Off-label Compendial uses

- No off-label uses meet evidence standards

### Coverage Guidelines

#### Crohn’s disease

**Initial authorization:**

The individual must meet all of the following criteria for approval:

- Does not have risk factors for the development of progressive multifocal leukoencephalopathy (PML) (i.e., patient immunocompromised, duration of therapy > 2 years, prior use of immunosuppressants [e.g., mitoxantrone, azathioprine, methotrexate, cyclophosphamide or mycophenolate mofetil], or presence of anti-JCV antibodies)
- Has moderately- to severely-active Crohn’s disease with evidence of inflammation
- Had an inadequate response to or is unable to tolerate conventional therapies and TNF-inhibitors
  - Conventional therapies include aminosalicylates (e.g., mesalamine, sulfasalazine), corticosteroids and immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, methotrexate)
  - TNF-inhibitors include: infliximab (Remicade®), adalimumab (Humira®), certolizumab pegol (Cimzia®)
- Patient will not be using Tysabri® (natalizumab) in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, methotrexate) or TNF-inhibitors

**Approval duration: 12 weeks**

**Reauthorization:**

The individual must meet all of the following criteria for approval:

- Has experienced therapeutic benefit by 12 weeks of induction therapy
- Has been tapered off chronic oral corticosteroids within 6 months of starting Tysabri® (natalizumab)
• Has no required additional steroid use that exceeds 3 months to control Crohn’s disease
• Does not have jaundice or other evidence of significant liver injury
• Has not developed an opportunistic infection

Multiple sclerosis

Initial authorization:
The individual must meet all of the following criteria for approval:
• Does not have risk factors for the development of progressive multifocal leukoencephalopathy (PML) (i.e., patient immunocompromised, duration of therapy > 2 years, prior use of immunosuppressants [e.g., mitoxantrone, azathioprine, methotrexate, cyclophosphamide or mycophenolate mofetil], or presence of anti-JCV antibodies)
• Has a relapsing form of multiple sclerosis
• Use Tysabri® (natalizumab) as monotherapy

Reauthorization:
The individual must meet both of the following for approval:
• Does not have jaundice or other evidence of significant liver injury
• Has not developed an opportunistic infection

Additional Information for Prescribers

*(Black Box Warning) Because of the risk of progressive multifocal leukoencephalopathy (PML), Tysabri® (natalizumab) is available only under a restricted distribution program, the TOUCH® prescribing program.
• Tysabri® (natalizumab) should be discontinued in an individual with jaundice or other evidence of significant liver disease. The individuals should be monitored for signs or symptoms of liver injury, including elevations in liver transaminases (AST, ALT) and total bilirubin
• Tysabri® may increase the risk of certain infections. The individual should be monitored for development of infections
• Life-threatening and fatal cases of herpes encephalitis and meningitis have occurred while on Tysabri® (natalizumab). Discontinue Tysabri® (natalizumab) if this occurs and treat appropriately

*Prescribers are alerted to these safety concerns via educational points in the program.
References


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Vectibix® (panitumumab) J9303

When requesting Vectibix® (panitumumab) the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

FDA-approved indication

- Colorectal Cancer

Approved Off-label Compendial uses

- None

Coverage Guidelines

Colorectal Cancer

- Adenocarcinoma histology
- Tumors express KRAS/NRAS wild-type gene
- The individual has advanced, metastatic or unresectable disease
- The individual has not previously failed treatment or experienced disease progression with either cetuximab or panitumumab
- Vectibix® (panitumumab) will be administered:
  - In combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin), FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen, or irinotecan OR
  - As a single agent
    - The individual did experience disease progression after prior treatment with fluoropyrimidine- [i.e. capecitabine (Xeloda), fluorouracil (5-FU)], oxaliplatin- (Eloxatin), and irinotecan- (Camptosar) containing regimen OR had an intolerance to intensive therapy (i.e. FOLFOX, FOLFIRI)

Additional Information for Prescribers

- The following is an important safety concern regarding the use of Vectibix® (panitumumab):
  - Dermatologic toxicities occurred in 90% of patients and were severe (NCI-CTC grade 3 and higher) in 15% of patients receiving Vectibix® (panitumumab) monotherapy.
    - The clinical manifestations included, but were not limited to, acneiform dermatitis, pruritus, erythema, rash, skin exfoliation, paronychia, dry skin, and skin fissures.
    - Withhold or discontinue Vectibix® (panitumumab) for dermatologic or soft-tissue toxicity associated with severe or life-threatening inflammatory or infectious complications.
Dose modifications for Vectibix® (panitumumab) concerning dermatologic toxicity are provided in the prescribing information cited below.

References

2. National Comprehensive Cancer Network Drugs & Biologics Compendium (NCCN Compendium®) Accessed August 8, 2016. http://www.nccn.org/professionals/drug_compendium/content/contents.asp Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™). ©2016 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org.

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Velcade® (bortezomib) J9041

When requesting Velcade® (bortezomib), the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**

- Multiple Myeloma<sup>1,2</sup>
- Non-Hodgkin’s Lymphoma- Mantle cell lymphoma<sup>1,2</sup>

**Approved Off-label Compendial uses**

- Solitary Plasmacytoma/Smoldering Myeloma<sup>2</sup>
- Systemic Light Chain Amyloidosis<sup>2,3</sup>
- Waldenström’s Macroglobulinemia/ Lymphoplasmacytic Lymphoma<sup>2,3</sup>
- Non-Hodgkin’s Lymphoma- Adult T-cell Leukemia/Lymphoma<sup>2</sup>
- Non-Hodgkin’s Lymphoma- Multicentric Castleman’s disease<sup>2</sup>

**Coverage Guidelines**

The individual does not have any of the following contraindications to therapy and meets the coverage criteria below:

- Hypersensitivity (not including local reactions) to mannitol, boron, or bortezomib
- Intrathecal administration of Velcade® (bortezomib)

**Multiple Myeloma<sup>1,2</sup>, Systemic Light Chain Amyloidosis<sup>2,3</sup>, Waldenström’s Macroglobulinemia<sup>2,3</sup>, or Lymphoplasmacytic Lymphoma<sup>2,3</sup>**
- Used as primary treatment, maintenance therapy, or for relapsed, progressive, or refractory disease.<sup>2</sup>

**Solitary Plasmacytoma/Smoldering Myeloma<sup>2</sup>**
- The disease has progressed to active (symptomatic) myeloma<sup>2</sup> and
- Used as primary treatment, maintenance therapy, or for relapsed, progressive, or refractory disease.<sup>2</sup>

**Non-Hodgkin’s Lymphoma**
- Mantle cell lymphoma<sup>1,2</sup>
  - As induction therapy or for relapsed, refractory, or progressive disease<sup>2</sup>
- Peripheral T-cell lymphoma not otherwise specified, anaplastic large cell lymphoma, angioimmunoblastic T-cell lymphoma, or enteropathy-associated T-cell lymphoma<sup>2</sup>
Second-line therapy for relapsed or refractory disease in a non-candidate for transplant\(^2\)

**Adult T-cell Leukemia/Lymphoma**\(^2\)
- For non-responders to first-line therapy in a non-candidate for transplant\(^2\)

**Multicentric Castleman’s disease**\(^2\)
- Subsequent therapy for disease that has progressed following treatment of relapsed, progressive, or refractory disease.\(^2\)

The approval duration is 12 months.

### Additional Information for Prescribers

Velcade\(^\circledast\) (bortezomib) has the following contraindications for use:
- Individuals with hypersensitivity (not including local reactions) to mannitol, boron, or bortezomib.
- Intrathecal administration of Velcade\(^\circledast\) (bortezomib)

### References

2. National Comprehensive Cancer Network Drugs & Biologics Compendium (NCCN Compendium\(^\circledast\)) Accessed February 16, 2016. [http://www.nccn.org/professionals/drug_compendium/content/contents.asp](http://www.nccn.org/professionals/drug_compendium/content/contents.asp). Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines\(^\rm{™}\)). ©2016 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines\(^\rm{™}\) and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to [NCCN.org](http://www.nccn.org).

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**Vidaza® (azacitidine) J9025**

When requesting Vidaza® (azacitidine), the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indication**

- Myelodysplastic Syndrome

**Approved Off-label Compendial use**

- Acute Myelogenous Leukemia

**Coverage Guidelines**

The individual does not have an advanced malignant hepatic tumor

**Acute Myelogenous Leukemia**

- For treatment of individuals 60 years of age or older as induction, post-remission or as maintenance therapy
- For treatment of individuals with relapsed or refractory disease who cannot tolerate more aggressive regimens

**Myelodysplastic Syndrome**

- The prognostic categories for Myelodysplastic Syndrome are defined as follows:
  - **Lower risk disease**: International Prognostic Scoring System (IPSS)= Low/Intermediate-1; Revised International Prognostic Scoring System (IPSS-R)= Very Low, Low, Intermediate; WHO-Based Prognostic Scoring System (WPSS)= Very Low, Low, Intermediate
  - **Higher risk disease**: IPSS=Intermediate-2, High; IPSS-R= Intermediate, High, Very High; WPSS=High, Very High
- Initial treatment in lower risk individuals with:
  - Symptomatic anemia, no del (5q) cytogenic abnormality, serum erythropoietin levels greater than 500 mU/mL and none of the following apply to the individual: ≤ 60 years of age with ≤ 5% marrow blasts, hypocellular marrow, HLA-DR15 positivity, PNH clone positivity, or STAT-3 mutant cytotoxic T cell clones
  - Clinically relevant thrombocytopenia, neutropenia or increased marrow blasts
- Treatment in lower risk individuals with symptomatic anemia with:
  - Serum erythropoietin levels less than or equal to 500 mU/mL and no response to erythropoietins alone (eg, epoetin alfa, darbapoetin alfa) and in combination with lenalidomide, and no response or intolerance to immunosuppressive therapy (eg, ATG, cyclosporin A)
Del (5q) cytogenic abnormality and no response or intolerance to lenalidomide, serum erythropoietin levels greater than 500 mU/mL and none of the following apply to the individual: ≤ 60 years of age with ≤ 5% marrow blasts, hypocellular marrow, HLA-DR15 positivity, PNH clone positivity, or STAT-3 mutant cytotoxic T cell clones

- Treatment in higher risk individuals who are:
  - nontransplant candidates
  - transplant candidates
- Treatment in higher risk individuals who had no response or relapsed after hemopoietic stem cell transplant

**Additional Information for Prescribers**

- None

**References**

2. National Comprehensive Cancer Network Drugs & Biologics Compendium (NCCN Compendium®) Accessed August 18, 2016. [http://www.nccn.org/professionals/drug_compendium/content/contents.asp](http://www.nccn.org/professionals/drug_compendium/content/contents.asp). Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™). ©2016 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to [NCCN.org](http://www.nccn.org).
Xgeva® (denosumab) injection J0897

When requesting Xgeva® (denosumab), the individual requiring treatment must be diagnosed with one of the following FDA-approved or approved off-label compendial requirements and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**

- Prevention of skeletal-related events in individuals with bone metastases from solid tumors
- Treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity
- Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy

**Approved Off-label Compendial uses**

- Breast cancer, invasive: used with calcium and vitamin D supplementation in addition to chemotherapy or endocrine therapy for bone metastases in individuals with an expected survival of ≥ 3 months and adequate renal function
- Kidney cancer: as a component of best supportive care for bony metastases
- Non-small cell lung cancer: for supportive therapy in individuals with bone metastases
- Prostate cancer: for prevention of skeletal-related events in men with castration-recurrent prostate cancer who have documented bone metastases and creatinine clearance (CrCl) greater than 30 mL/min
- Thyroid carcinoma:
  - Follicular carcinoma: for bone metastases
  - Hürthle cell carcinoma: for bone metastases
  - Medullary carcinoma: for bone metastases
  - Papillary carcinoma: for bone metastases
- Giant cell tumor of the bone:
  - As a single agent or combined with interferon alfa/peginterferon or radiation therapy for localized disease
  - As a single agent for metastatic disease

**Coverage Guidelines**

The individual meets all of the following criteria for approval:

- The individual does not have hypocalcemia (defined as a serum calcium or corrected calcium < 8.5 mg/dL).
- The individual does not have a CrCl ≤ 30 mL/min or serum creatinine > 3 mg/dL.
- The individual has one of the following diagnoses:
  - Bone metastases from a solid tumor
If the primary cancer diagnosis is breast cancer, then the individual must have an expected survival of 3 months or greater.3
If the primary cancer diagnosis is prostate cancer, then the individual must have castration recurrent prostate cancer.3
The primary cancer diagnosis is not multiple myeloma or other non-solid (hematologic) tumor1

- Giant cell tumor of bone
  - Xgeva® (denosumab) is being used in one of the following clinical scenarios:
    - As a single agent or combined with interferon alfa/peginterferon or radiation therapy for localized disease3
    - As a single agent for metastatic disease3

- Hypercalcemia of malignancy
  - The individual has tried and had an inadequate response to intravenous bisphosphonate therapy.1

Approval duration: 180 days

†Corrected calcium (XX.X mg/dL) = measured serum calcium (XX.0 mg/dL) + 0.8 (4.0 - serum albumin [XX.X g/dL]) where 4.0 represents the average albumin level in g/dL.

Additional Information for Prescribers†

- Xgeva® is contraindicated in individuals with hypocalcemia.
- Individuals with increasing renal dysfunction, most commonly with severe dysfunction (CrCl < 30 mL/min), and with inadequate/no calcium supplementation, are at increased risk of hypocalcemia.
- * Osteonecrosis of the jaw can occur in individuals receiving Xgeva®. An oral examination should be performed prior to starting Xgeva®. Symptoms should be monitored and invasive dental procedures avoided during Xgeva® treatment.
- * Atypical femoral fracture has been reported with Xgeva®. Individuals with thigh or groin pain should be evaluated to rule out a femoral fracture.

* Prescribers are alerted to these safety concerns via educational points in the program.


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Yervoy® (ipilimumab) J9228

When requesting Yervoy® (ipilimumab), the individual requiring treatment must be diagnosed with the following FDA-approved indications or approved compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**

**Melanoma**
- Unresectable or metastatic disease
- Adjuvant treatment of an individual with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who has undergone complete resection, including total lymphadenectomy

**Approved Off-label Compendial uses**

**Melanoma**
- Therapy for metastatic or unresectable disease
  - In combination with nivolumab as first-line therapy
  - As a single agent or in combination with nivolumab as second-line or subsequent therapy for disease progression for an individual with performance status of 0-2 if not previously used
    - May be used in a select individual who has experienced no significant toxicity during prior ipilimumab therapy and has not relapsed in less than 3 months
  - As a single agent
    - For stage IIIA with metastases > 1 mm (2B)
    - For stage IIIB-C disease with nodal metastases following a complete lymph node dissection (2B)
    - For nodal recurrence following complete lymph node dissection and/or complete resection (2B)

**Central Nervous System**
- Consider for single agent treatment for brain metastases with limited (1-3) metastatic lesions if active against primary tumor (melanoma) for recurrent disease
- Single agent treatment for brain metastases with multiple (>3) metastatic lesions if active against primary tumor (melanoma) for brain metastases in an individual with recurrent stable systemic disease

**Coverage Guidelines**

**Melanoma**
- Therapy for metastatic or unresectable disease
  - In combination with Opdivo® (nivolumab) as first-line therapy
In combination with Opdivo® (nivolumab) as second-line or subsequent therapy for disease progression for an individual with performance status of 0-2 if not previously used2

As a single agent as second-line or subsequent therapy for disease progression for an individual with performance status of 0-2 if not previously used2

- May be used in a select individual who has experienced no significant systemic toxicity during prior Yervoy® (ipilimumab) therapy and has not relapsed in less than 3 months2

- As a single agent2
  - For stage IIIA with metastases > 1 mm (2B)2
  - For stage IIIB-C disease with nodal metastases following a complete lymph node dissection (2B)2
  - For nodal recurrence following complete lymph node dissection and/or complete resection (2B)2

Central Nervous System

- Single agent treatment for brain metastases with limited (1-3) metastatic lesions if active against primary tumor (melanoma) for recurrent disease2
- Single agent treatment for brain metastases with multiple (>3) metastatic lesions if active against primary tumor (melanoma) for brain metastases in an individual with recurrent stable systemic disease2

The approval duration is 12 months.

Additional Information for Prescribers

Warning: Immune-Mediated Adverse Reactions

- * Yervoy (ipilimumab) can result in severe and fatal immune-mediated adverse reactions. These immune-mediated reactions may involve any organ system; however, the most common include enterocolitis, hepatitis, dermatitis (including toxic epidermal necrolysis), neuropathy, and endocrinopathy. The majority of these reactions initially manifested during treatment; however, a minority occurred weeks to months after discontinuing Yervoy (ipilimumab).1
- * Permanently discontinue Yervoy (ipilimumab) and initiate systemic high-dose corticosteroid therapy for severe immune-mediated reactions.1
- * Assess patients for signs and symptoms of enterocolitis, dermatitis, neuropathy, and endocrinopathy, and evaluate clinical chemistries, including liver function tests, adrenocorticotropic hormone (ACTH) level, and thyroid function tests, at baseline and before each dose.1

* Prescribers are alerted to the above safety concerns via educational points in the program.
References


2. National Comprehensive Cancer Network Drugs & Biologics Compendium (NCCN Compendium®) Accessed February 2, 2016. http://www.nccn.org/professionals/drug_compendium/content/contents.asp. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™). ©2016 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org.


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Zarxio™ (filgrastim-sndz) Injection J3490

When requesting Zarxio™ (filgrastim-sndz), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications or approved off-label compendial requirements and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

**FDA-approved indications**

- To decrease the incidence of infection, as manifested by febrile neutropenia, in an individual with a non-myeloid malignancy receiving myelosuppressive anti-cancer drug(s) associated with a significant incidence of severe neutropenia with fever
- To reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment for an individual with acute myeloid leukemia
- To reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in an individual with a non-myeloid malignancy undergoing myeloablative chemotherapy followed by bone marrow transplantation
- To mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis
- To reduce the incidence and duration of sequelae of severe neutropenia in a symptomatic individual with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia

**Approved Off-label Compendial uses**

- For treatment of chemotherapy-induced febrile neutropenia
- For mobilization of hematopoietic progenitor cells in the allogeneic transplant setting

**Coverage Guidelines**

For all indications:
The individual does not have a history of serious allergic reactions to pegfilgrastim

For prophylaxis of chemotherapy-induced febrile neutropenia

- The individual has a solid tumor or non-myeloid malignancy and
- The individual has experienced febrile neutropenia or dose-limiting neutropenic event with prior chemotherapy cycle or
- The individual has one of the following risk categories for febrile neutropenia:
  - For high risk for febrile neutropenia:
    - The intent of chemotherapy is curative/adjuvant or to prolong survival

The intent of chemotherapy is symptom management. The risk of febrile neutropenia is not due to the chemotherapy regimen. If risk of febrile neutropenia is due to the chemotherapy regimen, the use of less myelosuppressive chemotherapy or dose reduction is not an option.

- For intermediate risk for febrile neutropenia:4
  - The intent of chemotherapy is curative/adjuvant or
  - The intent of chemotherapy is to prolong survival or to manage symptoms. The risk of febrile neutropenia is not due to the chemotherapy regimen. If risk of febrile neutropenia is due to the chemotherapy regimen, the use of less myelosuppressive chemotherapy or dose reduction is not an option.

- For low risk of febrile neutropenia:4
  - The intent of chemotherapy is curative/adjuvant and
  - The individual is at significant risk for serious medical consequences of febrile neutropenia, including death

**For the treatment of chemotherapy-induced febrile neutropenia**³
- The individual has a solid tumor or non-myeloid malignancy and
- The individual has received filgrastim-sndz as prophylaxis or has risk factors for an infection associated complication (i.e. sepsis syndrome, age >65 years, severe neutropenia [absolute neutrophil count <100/mcL], neutropenia expected to be more than 10 days in duration, pneumonia, invasive fungal infection, other clinically documented infections, hospitalization at the time of fever, prior episode of febrile neutropenia)⁴

**For acute myeloid leukemia:**
- The individual is receiving induction or consolidation chemotherapy¹,²

**Additional Information for Prescribers**¹
- Contraindicated in an individual with a history of a serious allergic reaction to pegfilgrastim
- *Do not administer Zarxio™ (filgrastim-sndz) within the 24-hour period prior to chemotherapy
- * Administer Zarxio™ (filgrastim-sndz) at least 24 hours after chemotherapy

* Prescribers are alerted to this safety concern via educational points in the program.

**References**

3. National Comprehensive Cancer Network Drugs & Biologics Compendium (NCCN Compendium®) Accessed November 12, 2015. http://www.nccn.org/professionals/drug_compendium/content/contents.asp Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines™). ©2015 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines™ and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org.