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The eviCore Specialty Drug Management Solution includes a library of clinically-based criteria that covers a variety of therapeutic areas. The individual criteria for each specialty medication is developed and updated by an experienced clinical team comprised of PharmDs and board-certified physicians from the relevant specialty areas. This criteria is also subject to review and oversight by an eviCore-sponsored external Medical Advisory Board to ensure clinical accuracy and program consistency.

As part of eviCore’s development process, several standards have been established to ensure fair and consistent decision-making. This is accomplished through the application of relevant criteria and clinical policies in accordance with regulatory requirements as well as industry standards and client expectations.

One of eviCore’s standards is to develop criteria based on nationally-recognized clinical recommendations. eviCore evaluates national treatment guidelines (e.g., NCCN, ACR guidelines), FDA labeling, clinical compendia (such as Micromedex, NCCN Drug and Biologics, and Clinical Pharmacology) for inclusion into its criteria. Another standard is to require a minimum level of evidence for a specific clinical indication to be included in the coverage criteria. The minimum requirement is Category 2B for NCCN or level of evidence IIb along with a grade of recommendation B for Micromedex with supporting clinical evidence.

All drug-specific clinical criteria include an evaluation of the clinical evidence supporting medical necessity, indications for use, safety, efficacy and the potential for step-therapy.
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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**¹

**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)**
- A individual 2 years of age and older with active systemic juvenile idiopathic arthritis

**Approved Off-label Compendial uses**²
- 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
- Actemra® (tocilizumab) will not be used in combination with another biologic agent¹
- For Actemra® (tocilizumab) re-authorization request, the individual’s condition must have improved or stabilized with at least 6 months of therapy³
- 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)¹

**Rheumatoid Arthritis (initial authorization)**³,⁵
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 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

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

The individual meets one of the following for approval:

- Had an inadequate response or intolerance to prior biologic agent 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) or
- Had an inadequate response or intolerance (including contraindication) to methotrexate or leflunomide

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.

References

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
- Colorectal Adenocarcinoma
- Non-Small Cell Lung Cancer (NSCLC)
- Ovarian Cancer
- Renal Cell Carcinoma

**Approved Off-label Compendial uses**

- Intravitreal therapy for non-oncology indications
  - Neovascular (wet) age-related macular degeneration (AMD)
  - Macular edema secondary to:
    - Diabetes
    - Branch retinal vein occlusion (BRVO) or
    - Central retinal vein occlusion (CRVO)
  - Proliferative diabetic retinopathy
  - Neovascular glaucoma
  - Choroidal neovascularization secondary to
    - Pathologic myopia,
    - Angioid streaks/pseudoxanthoma elasticum, or
    - Ocular histoplasmosis syndrome (OHS)
  - Cystoid macular degeneration
  - Histoplasmosis retinitis
  - Proliferative diabetic retinopathy
  - Retinal neovascularization
  - Severe nonproliferative diabetic retinopathy
- Brain or Central Nervous system cancers
  - Adult intracranial ependymoma (excludes subependymoma and myxopapillary)
  - Anaplastic gliomas
- Breast cancer
- Sarcoma
- Malignant Neoplasm of Connective Tissue (171.0—171.9)
Coverage Guidelines

Intravitreal therapy for non-oncology indications
- Neovascular (wet) age-related macular degeneration (AMD)
- Macular edema secondary to:
  - Diabetes
  - Branch retinal vein occlusion (BRVO) or
  - Central retinal vein occlusion (CRVO)
- Proliferative diabetic retinopathy
- Neovascular glaucoma
- Choroidal neovascularization secondary to
  - Pathologic myopia,
  - Angioid streaks/pseudoxanthoma elasticum, or
  - Ocular histoplasmosis syndrome (OHS)
- Cystoid macular degeneration
- Histoplasmosis retinitis
- Proliferative diabetic retinopathy
- Retinal neovascularization
- Severe nonproliferative diabetic retinopathy

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

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

Avastin is indicated for the first- or second-line treatment of patients with metastatic carcinoma (mCRC) of the colon or rectum in combination with intravenous 5-fluorouracil-based chemotherapy.

- Treatment of resectable synchronous liver and or lung metastases1,2
  - Neoadjuvant therapy for patients with synchronous liver and/or lung metastases or with resectable metachronous metastases (NCCN compendium category 2A)
  - Used in combination with one of the following regimes:
    - FOLFOX (fluorouracil, leucovorin, and oxaliplatin),
    - FOLFIRI (fluorouracil, leucovorin, and irinotecan), or
    - CapeOX (capecitabine and oxaliplatin)
- Treatment of unresectable synchronous liver and/or lung metastases (NCCN compendium category 2A)2
  - Primary therapy for patients with unresectable synchronous liver and/or lung metastases, with synchronous abdominal/peritoneal metastases, or with unresectable metachronous metastases (NCCN compendium)
- Treatment of unresectable advanced or metastatic disease2
  - Initial therapy for patients with unresectable advanced or metastatic disease
    - For patient who can tolerate intensive therapy in combination with infusional 5-FU/LV in combination with one of the following regimens:
      - Capecitabine or with
      - FOLFOX (fluorouracil, leucovorin, and oxaliplatin),
      - FOLFIRI (fluorouracil, leucovorin, and irinotecan),
      - 5-FU/LV (fluorouracil and leucovorin), or
      - CapeOX (capecitabine and oxaliplatin)
    - For patients who cannot tolerate intensive therapy in combination with
      - Infusional 5FU/LV
- Used as therapy after first progression of advanced or metastatic disease2
  - In combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin), FOLFIRI
  - This agent can be used even if it was included in the failed initial regimen.1
- Not indicated in the adjuvant setting for stage II or III outside of the setting of a clinical trial (NCCN compendium)

Non-Small Cell Lung Cancer (NSCLC)

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

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

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

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

**Malignant Neoplasm of Connective Tissue**

**Additional Information for Prescribers**
- The safety of administering bevacizumab pre or post operatively, in combination with 5FU based regimens has not been adequately evaluated. There should be at least a 6 week interval between the last dose of bevacizumab and elective surgery and at least 6-8 weeks postoperatively. There is an increased risk of stroke and other
arterial events especially in age ≥ 65. The use of bevacizumab may interfere with wound healing.

References

1. Avastin (bevacizumab) FDA Prescribing Information. Accessed 1/31/2013
7. L31836, Local Coverage Determination (LCD) for Chemotherapy and Biologicals, CGS Administrators, (15202) Ohio, Accessed 8/01/2012
9. L29959 Local Coverage Determination (LCD) for Bevacizumab (AVASTIN®); First Coast Service Options (MAC Part B) (09102) Florida. Accessed 8/01/2012
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


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


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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**

- 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**

- None

**Coverage Guidelines**

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

A. Does not have ocular or periocular infection
B. Does not have active intraocular inflammation

**Additional Information for Prescribers**

- 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=IAAAAAA%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=IAAAAAA%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=IAAAAAA%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=IAAAAAA%3d%3d&)

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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**¹

- 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 neutropenia¹

**Approved Off-label Compendial uses**²

- None

**Coverage Guidelines**

For prophylaxis of chemotherapy-induced febrile neutropenia¹,³

- The individual has a solid tumor or non-myeloid malignancy¹,⁴ AND
- The individual has experienced febrile neutropenia or dose-limiting neutropenic event with prior chemotherapy cycle¹ OR
- Individual has one of the following risk categories for febrile neutropenia:
  - For high risk for febrile neutropenia:⁴
    - 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: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, the intent of chemotherapy is curative/adjuvant and individual is at significant risk for serious medical consequences of febrile neutropenia, including death⁴

**Additional Information for Prescribers**¹

- *Do not administer Granix within 24 hours prior to chemotherapy¹
* Prescribers are alerted to this safety concern via educational points in the program.

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**

- 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**

- 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\textsuperscript{1-10,12,13,18,19}

- Hypogammaglobulinemia\textsuperscript{16,18}
- Multiple myeloma\textsuperscript{13,14}
- Other primary humoral immunodeficiency\textsuperscript{1-10,12,13,18,19}
- Pediatric human immunodeficiency virus\textsuperscript{13,17}
- Severe combined immunodeficiencies\textsuperscript{1-10,12,13,18,19}
- Wiskott-Aldrich syndrome\textsuperscript{1-10,12,13,18,19}

- Pre- and post transplant
  - Prophylaxis to reduce transplant rejection before transplant\textsuperscript{13}
  - Prophylaxis to reduce transplant rejection after transplant\textsuperscript{13}
  - Treatment of acute rejection\textsuperscript{13}

Approval duration: 180 days

**Safety Criteria\textsuperscript{1-12,18,19}**

- 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**


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 through 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® (alemuzumab).

- Lemtrada® (alemuzumab) 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® (alemuzumab) infusion and for the first 3 days of each treatment course
- *The initiation of Lemtrada® (alemuzumab) 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® (alemuzumab)
- *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® (alemuzumab)
- *Administration of antiviral agent for herpetic prophylaxis is recommended starting on the first day of Lemtrada® (alemuzumab) dosing and continuing for a minimum of 2 months after completion of Lemtrada® (alemuzumab) 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


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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**¹

- Use following induction chemotherapy in acute myelogenous leukemia¹
- Use in mobilization and following transplantation of autologous peripheral blood progenitor cells¹
- Use in myeloid reconstitution after autologous bone marrow transplantation¹
- Use in myeloid reconstitution after allogeneic bone marrow transplantation¹
- Use in bone marrow transplantation failure or engraftment delay¹

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

- For prophylaxis of chemotherapy-induced febrile neutropenia³
- For treatment of chemotherapy-induced febrile neutropenia³
- Crohn’s disease²
- To enhance hepatitis B vaccination response²
- Metastatic melanoma²
- For treatment of pulmonary alveolar proteinosis²
- For metastatic renal cell carcinoma²
- To promote wound healing²
- Myelodysplastic syndrome²,³

**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 product¹

**For prophylaxis of chemotherapy-induced febrile neutropenia**³

- The individual has a solid tumor or non-myeloid malignancy⁴ and
- The individual has experienced febrile neutropenia or dose-limiting neutropenic event with prior chemotherapy cycle⁴ or

The individual has one of the following risk categories for febrile neutropenia:
- For high risk for febrile neutropenia:⁴
  - 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 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

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**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] 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).


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**


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[www.eviCore.com](http://www.eviCore.com)
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**¹

- 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 neutropenia¹

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

- For individuals undergoing mobilization of hematopoietic progenitor cells²
- For individuals undergoing bone marrow transplantation³,⁴

**Coverage Guidelines**

For all indications:
The individual does NOT have a history of serious allergic reactions to filgrastim (Neupogen)¹

**For prophylaxis of chemotherapy-induced febrile neutropenia**¹,³

- The individual has a solid tumor or non-myeloid malignancy⁴ **AND**
- The individual has experienced febrile neutropenia or dose-limiting neutropenic event with prior chemotherapy cycle⁴ **OR**

Individual has one of the following risk categories for febrile neutropenia:

- For high risk for febrile neutropenia:⁴
  - 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: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, the intent of chemotherapy is curative/adjuvant and individual is at significant risk for serious medical consequences of febrile neutropenia, including death⁴
**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**


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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**¹

- 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 fever¹
- To reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment for an individual with acute myeloid leukemia¹
- 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 transplantation¹
- To mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis¹
- To reduce the incidence and duration of sequelae of severe neutropenia in a symptomatic individual with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia¹
- To increase survival in an individual acutely exposed to myelosuppressive doses of radiation

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

- For treatment of chemotherapy-induced febrile neutropenia³
- To revere neutropenia caused by human immunodeficiency virus (HIV) infection²
- For an individual undergoing esophagectomy²
- Myelodysplastic syndrome²,³
- For leukemia relapse after allogeneic stem cell transplantation²

**Coverage Guidelines**

**For all indications:**
The individual does not have a history of a serious allergic reaction to pegfilgrastim¹

**For prophylaxis of chemotherapy-induced febrile neutropenia**¹-³

- The individual has a solid tumor or non-myeloid malignancy¹,⁴ and
- The individual has experienced febrile neutropenia or dose-limiting neutropenic event with prior chemotherapy cycle⁴ or
- The individual has one of the following risk categories for febrile neutropenia:
  - For high risk for febrile neutropenia:⁴
• 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: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 treatment of chemotherapy-induced febrile neutropenia:3
• The individual has a solid tumor or non-myeloid malignancy or 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)4

For myelodysplastic syndrome:2,3
• 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 alfa

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

Additional Information for Prescribers1

• 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).

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 agent\(^1\)
- For Orencia® (abatacept) reauthorization request, the individual’s condition must have improved or stabilized with at least 6 months of therapy\(^3\)
- 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 DMARD\(^3,4\) **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 DMARD\(^3,4\)
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


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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 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% 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 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 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% 8 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

Prevention7 or treatment of bone loss in men with prostate cancer1
• The patient is at high risk for fracture, defined as:
  ▪ History of an osteoporotic fracture1
  ▪ 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 therapy1

Treatment of bone loss in women with breast cancer1
• The patient is at high risk for fracture, defined as:
  ▪ History of an osteoporotic fracture1
  ▪ 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 therapy1

Safety Criteria (for all approved indications)1
• 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

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 \( \leq -2.5 \) by dual-energy x-ray absorptiometry (DXA)
    - The patient has had an history of osteoporotic fractures
  - 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 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 treatment:1
    - Reclast (zoledronic acid) dosing: a single 5mg infusion1
  - For retreatment:1
    - 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

The patient is symptomatic

Reclast (zoledronic acid) dosing: a single 5mg infusion

Reclast® (zoledronic acid) - For all indications

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

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

†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.)

‡ 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:

§A fracture caused by injury that would be insufficient to fracture normal bone.

Zometa® (zoledronic acid)

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

- Multiple myeloma
  - 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

- Bone metastases from solid tumors
  - The patient’s primary cancer diagnosis is prostate cancer
    - The patient has castration-recurrent prostate cancer
Reclast® and Zometa® (zoledronic acid) Injection J3487, J3488, J3489, Q2051

Zometa (zoledronic acid) will be used in conjunction with standard antineoplastic therapy6
- Zometa (zoledronic acid) dosing: up to 4 mg (depending on CrCl) every 3 to 4 weeks6
  - The patient’s primary cancer diagnosis is something other than prostate cancer8
    - Zometa (zoledronic acid) will be used in conjunction with standard antineoplastic therapy6
    - Zometa (zoledronic acid) dosing: up to 4 mg (depending on CrCl) every 3 to 4 weeks6

- Monoclonal gammopathy of uncertain significance with osteopenia or osteoporosis7
  - Zometa (zoledronic acid) dosing: 4 mg every 6 months7

- Prevention or treatment of osteoporosis during androgen deprivation therapy7,8
  - The patient is at high risk for fractures8
  - Zometa (zoledronic acid) dosing: 4 mg every 3 months7

- Osteopenia, secondary to hormone therapy in breast cancer patients7
  - Zometa (zoledronic acid) dosing: 4 mg every 6 months7

- 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 months7

*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® algorithm9

Additional Information for Prescribers

- None

References


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# 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)**
  - The individual meets the following criteria for approval:
    - Remicade® (infliximab) will be taken in combination with methotrexate and
    - Has had an inadequate response or intolerance to a prior biologic agent or
    - Has moderately- to severely-active rheumatoid arthritis and has tried and had an inadequate response, intolerance or contraindication to at least one non-biologic disease modifying antirheumatic drug (DMARD)
    - Or
    - Has poor prognostic factors such as functional limitation, extraarticular disease, positive rheumatoid factor or anti-cyclic citrullinated peptide antibodies, or bony erosions by radiograph and
    - Has tried and had an inadequate response, intolerance or contraindication to at least one non-biologic disease modifying antirheumatic drug (DMARD)
- **Moderately-to severely-active psoriatic arthritis**
- **Active ankylosing spondylitis**
  - The individual has had an inadequate response, intolerance, or contraindication to non-steroidal anti-inflammatory drugs (NSAIDs)
- **Chronic, severe plaque psoriasis**
  - The individual has an inadequate response, intolerance, or contraindication to either phototherapy or oral conventional systemic therapy (e.g., methotrexate, cyclosporine, acitretin)
- **Crohn’s disease**
  - 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.)
- **Ulcerative colitis**
  - 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-mecaptopurine, etc.)
The prescribed drug is being requested for one of the following compendial uses:

- 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/kg¹
- Does not have an active infection (including active tuberculosis or any clinically important localized infection)¹
- Remicade® (infliximab) will not be used in combination with another biologic agent¹
- Has been screened for latent TB infection¹
- Is negative for latent TB infection. Or if positive, has started or will be treated for latent TB prior to starting Remicade® (infliximab)¹
- Has been tested for hepatitis B virus (HBV) and if appropriate, HBV infection has been ruled out or treatment initiated¹

Reauthorization request for Remicade® (infliximab) therapy and the prescribed indication is one of the following is one of the following¹,³:

- 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® (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/kg¹
2. Does not have an active infection (including active tuberculosis or any clinically important localized infection)\(^1\)

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

*Methotrexate, Hydroxychloroquine, Sulfasalazine, etc.

**Additional Information for Prescribers**

An individual treated with Remicade\(^\circledast\) (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\(^\circledast\) (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\(^\circledast\) (infliximab) use and during therapy. Treatment for latent infection should be initiated prior to Remicade\(^\circledast\) (infliximab) use.
- Invasive fungal infections including histoplasmosis, coccidioidomycosis, 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\(^\circledast\) (infliximab) should be carefully considered prior to initiating therapy in an individual with chronic or recurrent infection.

Remicade\(^\circledast\) (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\(^\circledast\) (infliximab) in patients with moderate to severe heart failure (New York Heart Association [NYHA] Functional Class III/IV), Remicade\(^\circledast\) (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\(^\circledast\) (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\(^1\)
• 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\(^1\)
• Use Tysabri\(^\circledast\) (natalizumab) as monotherapy\(^1\)

Reauthorization:
The individual must be 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\(^1\)**

*(Black Box Warning)* Because of the risk of progressive multifocal leukoencephalopathy (PML), Tysabri\(^\circledast\) (natalizumab) is available only under a restricted distribution program, the TOUCH\(^\circledast\) prescribing program.
• Tysabri\(^\circledast\) (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 is liver transaminases (AST, ALT) and total bilirubin
• Tysabri\(^\circledast\) 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\(^\circledast\) (natalizumab). Discontinue Tysabri\(^\circledast\) (natalizumab) if this occurs and treat appropriately

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


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 hypocalemia.
- 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 hypocalemia.
- * 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.
References


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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 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 the treatment of chemotherapy-induced febrile neutropenia:
- 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)

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 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
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