Clinical Policy: Step Therapy

Reference Number: MCPB.ST.00
Effective Date: 01.01.21
Last Review Date: 08.21
Line of Business: Medicare Part B

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
This policy provides a list of drugs that require step therapy. Step therapy is when we require the trial of a preferred therapeutic alternative prior to coverage of a non-preferred drug for a specific indication.

FDA Approved Indication(s)
Various.

Policy/Criteria
This policy does not replace existing Medicare rules and regulations for the applicable agent(s).

I. Approval Criteria (NEW STARTS ONLY – member has not received the drug for the past 365 days)

A. Step Therapy:

Drug Name	Required Step-Through Agents* By Indication **May require prior authorization*
Abatacept (Orencia®)	• **Rheumatoid arthritis**: two of the following: Enbrel*, Humira*, Rinvoq*, Xeljanz*/Xeljanz XR* • **Polyarticular juvenile idiopathic arthritis**: two of the following: Enbrel*, Humira*, Xeljanz* • **Psoriatic arthritis**: two* of the following: Enbrel*, Humira*, Xeljanz*/Xeljanz XR*
Aflibercept (Eylea®)	• **Neovascular (wet) age-related macular degeneration (AMD), macular edema following retinal vein occlusion (RVO), diabetic macular edema (DME), or diabetic retinopathy (DR)**: intravitreal bevacizumab solution
Atezolizumab (Tecentriq®)	• **Urothelial carcinoma**: member is ineligible for platinum-containing chemotherapy as first-line systemic therapy* (*note some IV chemo may not require prior authorization*) • **Non-small cell lung cancer**: ○ If anaplastic lymphoma kinase (ALK) or epidermal growth factor receptor (EGFR) mutation negative or unknown, prior platinum-containing chemotherapy (*note some IV chemo*

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	may not require prior authorization), unless any of the following are met: ▪ Request is for use as a single agent as first-line therapy for tumors that have high programmed death-ligand 1 (PD-L1) expression, defined as PD-L1 ≥ 50% (tumor cells [TC] ≥ 50%) or tumor-infiltrating immune cells (IC) covering ≥ 10% of the tumor area [IC ≥ 10%] ▪ Disease is non-squamous, and Tecentriq is prescribed as combination therapy ▪ No prior progression on a programmed death receptor-1 (PD-1) or PD-L1 inhibitor (e.g., Tecentriq, nivolumab, pembrolizumab, durvalumab), and Tecentriq is prescribed as single agent as subsequent therapy o If ALK or EGFR mutation positive: ALK-mutation therapy (e.g., Xalkori*, Alecensa*, Zykadia*) or EGFR-mutation therapy* (e.g., Tarceva*, Gilotrif*, Iressa*)
Axicabtagene ciloleucel (Yescarta®)	• **Large B-cell lymphoma**: 2 lines of systemic therapy that includes rituximab* and one anthracycline-containing regimen (e.g., doxorubicin) • **Relapsed or refractory follicular lymphoma:** 2 lines of systemic therapy that includes a combination of an anti-CD20 monoclonal antibody* (e.g., rituximab or Gazyva) and an alkylating agent (e.g., bendamustine, cyclophosphamide, chlorambucil) *Only for initial treatment dose; subsequent doses will not be covered*
Bevacizumab (Avastin®, Mvasi®, Zirabev™)	• **Oncology indications**, if request is for Avastin: Mvasi or Zirabev
Brexucabtagene autoleucel (Tecartus™)	• **Mantle cell lymphoma**: 2 to 5 prior regimens that included all of the following: anthracycline (e.g., doxorubicin*) or bendamustine*-containing chemotherapy; anti-CD20 monoclonal antibody therapy (e.g., rituximab*); and Bruton tyrosine kinase (BTK) inhibitor (e.g., Imbruvica*, Calquence*, Brukinsa*) *Only for initial treatment dose; subsequent doses will not be covered*
Brolucizumab-dbll (Beovu®)	• **Neovascular (wet) AMD**: intravitreal bevacizumab solution

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Buprenorphine implant/ injection (Probuphine®, Sublocade®)	• **Opioid dependence**: oral buprenorphine or buprenorphine/naloxone sublingual tablet or film
Certolizumab (Cimzia®)	• **Crohn's disease**: a different TNF inhibitor (e.g., infliximab*, Humira*) • **Rheumatoid arthritis**: two of the following: Enbrel*, Humira*, Rinvoq*, Xeljanz*/Xeljanz XR* • **Psoriatic arthritis**: two of the following: Enbrel*, Humira*, Xeljanz*/Xeljanz XR* • **Ankylosing spondylitis:** a different TNF inhibitor (e.g., infliximab*, Humira*, Enbrel*) • **Plaque psoriasis**: two of the following: Enbrel*, Humira*, Skyrizi*
Corticosteroid intravitreal implants: dexamethasone (Ozurdex®), fluocionolone acetonide (Iluvien®, Retisert®, Yutiq™)	• **Macular edema following branch or central RVO (*Ozurdex only*)**: intravitreal bevacizumab solution • **Non-infectious uveitis affecting the posterior segment of the eye (*Ozurdex, Retisert, or Yutiq*)**: systemic corticosteroid (e.g., predisone) and non-biologic immunosuppressive therapy (e.g., azathioprine, chlorambucil, cyclophosphamide, cyclosporine, methotrexate, mycophenolate mofetil, tacrolimus) • **DME (*Ozurdex or Iluvien*)**: intravitreal bevacizumab solution
Corticotropin (H.P. Acthar®)	• **Multiple sclerosis**: corticosteroid and multiple sclerosis treatment (e.g., Aubagio*, Tecfidera*, Gilenya*, Avonex*, Betaseron*, Plegridy*, glatiramer*, Copaxone*, Glatopa*)
Crizanlizumab-tmca (Adakveo®)	• **Sickle cell disease**: hydroxyurea and L-glutamine*
Daratumumab (Darzalex®)	• **Multiple myeloma**: 1 prior systemic therapy (e.g., ixazomib*, bortezomib*, carfilzomib*, lenalidomide*, thalidomide) (*note some IV chemo may not require prior authorization*) if prescribed in combination with dexamethasone and either lenalidomide*, bortezomib*, or carfilzomib*; OR 2 prior systemic therapies (an immunodulatory agent [e.g., thalidomide*, lenalidomide*] and a proteasome inhibitor [e.g., ixazomib*, bortezomib*, carfilzomib*]) if prescribed as monotherapy or in combination with pomalidomide* and dexamethasone; UNLESS Darzalex is prescribed as primary therapy in one of the following ways:

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	○ In combination with lenalidomide* and dexamethasone or bortezomib*, melphalan*, and prednisone, and member is ineligible for autologous stem cell transplant (ASCT); or ○ In combination with bortezomib*, thalidomide*, and dexamethasone, and member is eligible for ASCT • **Systemic light chain amyloidosis**: 1 prior systemic therapy (e.g., bortezomib*, lenalidomide*) (*note some IV chemo may not require prior authorization*)
Denosumab (Xgeva®)	• **Systemic mastocytosis, hypercalcemia of malignancy**: zoledronic acid* or pamidronate*
Durvalumab (Imfinzi®)	• **Non-small cell lung cancer**: chemotherapy (e.g., platinum-containing chemotherapy)* (*note some IV chemo may not require prior authorization*)
Eculizumab (Soliris®)	• **Generalized myasthenia gravis**: one corticosteroid, one cholinesterase inhibitor (e.g., neostigmine*, pyridostigmine*), and two immunosuppressive therapies (e.g., azathioprine, mycophenolate, cyclosporine, rituximab*) • **Neuromyelitis optica spectrum disorder**: rituximab*
Elotuzumab (Empliciti®)	• **Multiple myeloma**: prior line of systemic therapy (e.g., bortezomib*, Revlimid*, Pomalyst*) (*note some IV chemo may not require prior authorization*)
Emapalumab-lzsg (Gamifant™)	• **Primary hemophagocytic lymphohistiocytosis (HLH)**: conventional HLH therapy that includes an etoposide- and dexamethasone-based regimen* (*note some IV chemo may not require prior authorization*)
Esketamine (Spravato™)	• **Treatment-resistant depression**: two antidepressants (e.g., selective serotonin reuptake inhibitor [SSRI], serotonin-norepinephrine reuptake inhibitor [SNRI], tricyclic antidepressant [TCA], bupropion, mirtazapine) from two different classes
Eteplirsen (Exondys 51™)	• **Duchenne muscular dystrophy**: oral corticosteroid (e.g., prednisone, Emflaza*)
Filgrastim (Neupogen®, Zarxio®, Nivestym™, Granix®)	• **All indications**, if request is for an agent other than Zarxio: Zarxio ○ If unable to use Zarxio and request is for Neupogen: biosimilar filgrastim product (e.g., Nivestym, Granix)
Golimumab (Simponi®, Simponi Aria®)	• **Rheumatoid arthritis**: two of the following: Enbrel*, Humira*, Rinvoq*, Xeljanz*/Xeljanz XR*

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	• **Psoriatic arthritis**: two of the following: Enbrel*, Humira*, Xeljanz*/Xeljanz XR* • **Ankylosing spondylitis**: a different TNF inhibitor* (e.g., infliximab*, Humira*, Enbrel*) • **Polyarticular juvenile idiopathic arthritis**: two of the following: Enbrel*, Humira*, Xeljanz* • **Ulcerative colitis**: Humira* and Xeljanz/Xeljanz XR*
Golodirsen (Vyondys 53™)	• **Duchenne muscular dystrophy**: oral corticosteroid (e.g., prednisone, Emflaza*)
Hyaluronate derivatives: sodium hyaluronate (Euflexxa®, Gelsyn-3™, GenVisc®850, Hyalgan®, Supartz™, Supartz FX™, Synojoynt™, Triluron™, TriVisc™, VISCO-3™), hyaluronic acid (Durolane®), cross-linked hyaluronate (Gel-One®), hyaluronan (Hymovis®, Orthovisc®, Monovisc®), hylan polymers A and B (Synvisc®, Synvisc One®)	• **Osteoarthritis of the knee**: simple analgesics (e.g., acetaminophen or nonsteroidal anti-inflammatory drugs [NSAIDs]) and intra-articular glucocorticoid injection*, and: ○ If request is for a product other than Synvisc/Synvisc One or Euflexxa: Synvisc*/Synvisc One* or Euflexxa*
Immune globulins (Asceniv™, Bivigam®, Carimune® NF, Cutaquig®, Cuvitru™, Flebogamma® DIF, GamaSTAN®, GamaSTAN® S/D, Gammagard® liquid, Gammagard® S/D, Gammaked™, Gammaplex®, Gamunex®-C, Hizentra®, HyQvia®, Octagam®, Panzyga®, Privigen®, Xembify®)	• **<u>ALL INDICATIONS</u> except viral prophylaxis for hepatitis A, measles, varicella, or rubella viruses**, if request is for an agent other than Gammagard: Gammagard* <u>IN ADDITION:</u> • **Chronic idiopathic demyelinating polyneuropathy**: a systemic corticosteroid (e.g., prednisone) • **Dermatomyositis**: a systemic corticosteroid (e.g., prednisone) in combination with one of the following immunosuppressive agents: methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil, tacrolimus, or cyclosporine; and rituximab* • **Polymyositis**: a systemic corticosteroid (e.g., prednisone) in combination with one of the following immunosuppressive agents: methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil, tacrolimus, or cyclosporine • **Idiopathic thrombocytopenic purpura**: a systemic corticosteroid or Rho(D) immune globulin* • **Multiple sclerosis**: three FDA-approved disease-modifying MS therapies (e.g., Aubagio*, Tecfidera*,

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	Gilenya*, Avonex*, Betaseron*, Plegridy*, glatiramer*, Copaxone*, Glatopa*) • **Myasthenia gravis/Lambert Eaton myasthenic syndrome**: amifampridine* (for Lambert Eaton myasthenic syndrome) or cholinesterase inhibitor (e.g., neostigmine*, pyridostigmine*; for myasthenia gravis), AND systemic corticosteroid and immunosuppressant (e.g., azathioprine) • **Opsoclonus-myoclonus syndrome**: one systemic corticosteroid • **Pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid (a.k.a. cicatricial pemphigoid), or epidermolysis bullosa acquisita**: one corticosteroid (e.g., prednisone), one immunosuppressive agent (e.g., azathioprine, mycophenolate mofetil, cyclophosphamide), and rituximab* • **Adenosine deaminase (ADA)-severe combined immunodeficiency disorders (SCID)**: Adagen* or Revcovi* • **Stiff person syndrome**: a benzodiazepine or baclofen
Infliximab (Remicade®, Avsola™, Renflexis™, Inflectra®)	• **ALL INDICATIONS:** if request is Remicade: Avsola*, Inflectra*, and Renflexis* IN ADDITION: • **Rheumatoid arthritis**: one of the following: methotrexate, sulfasalazine, hydroxychloroquine, d-penicillamine, azathioprine, or auranofin • **Plaque psoriasis**: one of the following: methotrexate, cyclosporine, or acitretin
Luspatercept-aamt (Reblozyl®)	• **Myelodysplastic syndrome:** erythropoiesis-stimulating agent used in combination with a granulocyte colony stimulating factor, unless current serum erythropoietin is greater than 500 mU/mL
Mometasone furoate sinus implant (Sinuva®)	• **Nasal polyps**: 2 intranasal steroids
Natalizumab (Tysabri®)	• **Crohn's disease**: adalimumab* and infliximab* • **Relapsing-remitting multiple sclerosis**: one disease modifying therapy (e.g., Aubagio*, Tecfidera*, Gilenya*, Avonex*, Betaseron*, Plegridy*, glatiramer*, Copaxone*, Glatopa*)
Ocrelizumab (Ocrevus®)	• **Relapsing-remitting multiple sclerosis**: one disease modifying therapy (e.g., Aubagio*, Tecfidera*,

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	Gilenya*, Avonex*, Betaseron*, Plegridy*, glatiramer*, Copaxone*, Glatopa*)
Omalizumab (Xolair®)	• **Asthma**: inhaled corticosteroid (e.g., beclomethasone, budesonide, flunisolide, fluticasone, mometasone, ciclesonide) • **Chronic idiopathic urticaria**: H1 antihistamine (e.g., levocetirizine, desloratadine)
OnabotulinumtoxinA (Botox®)	• **Upper limb spasticity, cervical dystonia, blepharospasm:** Xeomin* • **Chronic migraine**: one migraine preventative therapy (an anticonvulsant, beta blocker, or antidepressant [e.g., divalproex, propranolol, or amitriptyline]) and one of the following abortive therapies: sumatriptan, rizatriptan, zolmitriptan, naratriptan, almotriptan, frovatriptan, eletriptan, ergotamine/caffeine, or dihydroergotamine)
Pegaptanib (Macugen®)	• **Neovascular (wet) AMD**: intravitreal bevacizumab solution

Pegfilgrastim (Neulasta®, Fulphila™, Nyvepria™, Udenyca™, Ziextenzo™)	• **All indications**: Zarxio*, unless member requires ≥ 10 doses of Zarxio, member is unable to self-administer Zarxio due to lack of caregiver or support system for assistance with administration and inadequate access to healthcare facility or home care interventions
	  ○ If unable to use Zarxio for any of the reasons listed above and request is for an agent other than Ziextenzo: Ziextenzo*
	  ▪ If unable to use Ziextenzo and request is for Neulasta: biosimilar pegfilgrastim product (e.g., Fulphila, Nyvepria, Udenyca)*

Pegloticase (Krystexxa®)	• **Chronic gout**: allopurinol, Uloric*, and a uricosuric agent (e.g., probenecid, losartan)
Ramucirumab (Cyramza®)	• **Esophageal, esophagogastric junction, and gastric cancer**: prior lines of systemic therapy* (*note some IV chemo may not require prior authorization*) • **Hepatocellular carcinoma**: Nexavar*
Ranibizumab (Lucentis®)	• **Neovascular (wet) AMD, macular edema following RVO, DME, DR, or myopic choroidal neovascularization (mCNV)**: intravitreal bevacizumab solution
Reslizumab (Cinqair®)	• **Asthma**: an inhaled corticosteroid used in combination with a long-acting beta-agonist (e.g.,

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	fluticasone-salmeterol, fluticasone-vilanterol, mometasone-formoterol)
Rituximab (Rituxan®, Riabni™, Ruxience™, Truxima®), rituximab/ hyaluronidase (Rituxan Hycela™)	• **All indications**, if request is for an agent other than Ruxience: Ruxience* • **All oncology indications**, if request is for Rituxan Hycela: member has received at least one full dose of Rituxan, Riabni, Ruxience, or Truxima • **Rheumatoid arthritis**, if request is for Rituxan or Truxima: infliximab*
Romiplostim (Nplate®)	• **Immune thrombocytopenia**: systemic corticosteroid (if intolerant or contraindicated to systemic corticosteroids, then immune globulin*) • **Myelodysplastic syndrome**: hypomethylating agent (e.g., azacitadine*, decitabine*) or immunosuppressive therapy (e.g., Atgam*, cyclosporine)
Romosuzumab-aqqg (Evenity™)	• **Postmenopausal osteoporosis**: bisphosphonate, unless member is very high risk for fracture (BMD T-score at hip or spine ≤ -3.5, OR BMD T-score at hip or spine ≤ -2.5 and major osteoporotic fracture [i.e., hip, spine, forearm, wrist, humerus])
Sargramostim (Leukine®)	• **All indications**: Zarxio
Sipuleucel-T (Provenge®)	• **Prostate cancer**: androgen deprivation therapy (e.g., Zoladex*, Vantas*, leuprolide*, Trelstar*, bicalutamide*, flutamide*, nilutamide*, Xtandi*, Erleada*, Nubeqa*, Firmagon*)
Teprotumumab-trbw (Tepezza™)	• **Thyroid eye disease**: a systemic corticosteroid
Tisagenlecleucel (Kymriah®)	• **B-cell precursor acute lymphoblastic leukemia**: at least two prior systemic therapy* *Only for initial treatment dose; subsequent doses will not be covered* • **Large B-cell lymphoma**: 2 lines of systemic therapy that includes rituximab* and one anthracycline-containing regimen (e.g., doxorubicin*) *Only for initial treatment dose; subsequent doses will not be covered*
Tocilizumab (Actemra®)	• **Rheumatoid arthritis**: two* of the following: Enbrel, Humira, Rinvoq, Xeljanz/Xeljanz XR • **Giant cell arteritis**: methotrexate or azathioprine • **Polyarticular juvenile idiopathic arthritis**: two* of the following: Enbrel, Humira, Xeljanz

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Trastuzumab (Herceptin®, Ontruzant®, Herzuma®, Ogivri™, Trazimera™, Kanjinti™), trastuzumab/hyaluronidase (Herceptin Hylecta™)	• **All indications**, if request is for an agent other than Ogivri or Trazimera: Ogivri* or Trazimera*
Triamcinolone ER injection (Zilretta®)	• **Osteoarthritis of the knee**: oral NSAID (or topical NSAID* if age ≥ 75 years or unable to take an oral NSAID) and intra-articular glucocorticoid injection
Ustekinumab (Stelara®)	• **Psoriatic arthritis**: two of the following: Enbrel*, Humira*, Xeljanz*/Xejanz XR* • **Crohn's disease**: a TNF inhibitor (e.g., infliximab*, Humira*) • **Plaque psoriasis**: two of the following: Enbrel*, Humira*, Skyrizi* • **Ulcerative colitis**: Humira* and Xeljanz*/Xeljanz XR*
Vedolizumab (Entyvio®)	• **Ulcerative colitis**: two of the following: Humira*, Xeljanz*/Xeljanz XR*, infliximab*/infliximab biosimilar* • **Crohn's disease**: Humira* and infliximab*/infliximab biosimilar*
Verteporfin (Visudyne®)	• **Classic subfoveal CNV due to AMD, pathologic myopia, or presumed ocular histoplasmosis**: intravitreal bevacizumab solution
Viltolarsen (Viltepso®)	• **Duchenne muscular dystrophy**: oral corticosteroid (e.g., prednisone, Emflaza*)

For questions, please reach out to your provider relations.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on FDA recommendation(s), peer-reviewed medical literature and evidence-based clinical practice guidelines.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan or responsible business unit. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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