Market Applicability						
Market	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	NA

Avsola (infliximab-axxq) Inflectra (infliximab-dyyb), Remicade (infliximab), Renflexis (infliximab-abda)

Override(s)	Approval Duration
Prior Authorization	1 year

Medications	Dosing Limit
Avsola (infliximab-axxq) 100 mg vial Inflectra (infliximab-dyyb) 100 mg vial Remicade (infliximab) 100 mg vial Renflexis (infliximab-abda) 100 mg vial	10 mg/kg as frequently as every 8 weeks

Dosing Override Criteria:

I. For initiation of therapy, may approve up to 5 mg/kg at weeks 0, 2, and 6.
II. For Ankylosing Spondylitis (AS) and Plaque Psoriasis (Ps), may approve 5 mg/kg as frequent as every 6 weeks (Label, AAD).
III. For Rheumatoid Arthritis (RA), Crohn's Disease (CD), Ulcerative Colitis (UC), or non-infectious uveitis (UV) may approve as frequent as every 4 weeks (Label, AGA, Levy-Clarke 2014).

APPROVAL CRITERIA

STEP THERAPY APPROVAL CRITERIA

Requests for Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda) may be approved when the following criteria **AND** prior authorization criteria listed below are met.

I. Individual has had a trial (medication samples/coupons/discount cards are excluded from consideration as a trial) and inadequate response or intolerance to Avsola (infliximab-axxq);

OR

II. Individual has been receiving the requested infliximab product [Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda)];
AND

This policy does not apply to health plans or member categories that do not have pharmacy benefits, nor does it apply to Medicare. Note that market specific restrictions or transition-of-care benefit limitations may apply.

Market Applicability						
Market	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	NA

III. Individual has previously undergone at least one switch between infliximab agents [reference (Remicade) or biosimilar agents (Avsola, Inflectra, Renflexis)].

PRIOR AUTHORIZATION APPROVAL CRITERIA

Avsola (infliximab-axxq), Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda) may be approved the following criteria are met:

I. Crohn's disease (CD) when each of the following criteria are met:
   A. Individual is 6 year of age or older with fistulizing or moderate to severe (CD) ; **AND**
   B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy (such as 5-Aminosalicylic acid products, systemic corticosteroids, or immunosuppressants);

OR

II. Ulcerative colitis (UC) when each of the following criteria are met:
   A. Individual is 6 years of age or older with moderate to severe UC; **AND**
   B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy (such as 5-Aminosalicylic acid products, systemic corticosteroids, or immunosuppressants);

OR

III. Rheumatoid arthritis (RA) when each of the following criteria are met:
   A. Individual is 18 years of age or older with moderate to severe RA; **AND**
   B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy [nonbiologic disease modifying anti-rheumatic drugs (DMARDs) (such as methotrexate, sulfasalazine, leflunomide, or hydroxychloroquine)] (ACR 2015);

OR

IV. Ankylosing spondylitis (AS) when each of the following criteria are met:
   A. Individual is 18 years of age or older with moderate to severe AS; **AND**
   B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy [such as NSAIDs or nonbiologic disease modifying anti-rheumatic drugs (DMARDs) (such as sulfasalazine)] (ACR 2019);

OR

V. Psoriatic arthritis (PsA) when each of the following criteria are met:
   A. Individual is 18 years of age or older with moderate to severe PsA; **AND**
   B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy [nonbiologic disease modifying anti-rheumatic drugs (DMARDs) (such as methotrexate, sulfasalazine, or leflunomide)];

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OR

VI. Plaque psoriasis (Ps) (Psoriasis vulgaris) when each of the following criteria are met:
   A. Individual is 18 years of age or older with chronic moderate to severe (that is, extensive or disabling) plaque Ps (psoriasis vulgaris) with either of the following (AAD 2019):
      1. Plaque Ps (psoriasis vulgaris) involving greater than three percent (3%) body surface area (BSA); **OR**
      2. Plaque Ps (psoriasis vulgaris) involving less than or equal to three percent (3%) BSA involving sensitive areas or areas that significantly impact daily function (such as palms, soles of feet, head/neck, or genitalia); **AND**
   B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to phototherapy or other systemic therapies (such as acitretin, cyclosporine, or methotrexate);

OR

VII. Polyarticular juvenile idiopathic arthritis (PJIA) when each of the following criteria are met (DP B IIb, Lahdenne 2003, Gerloni 2005):
   A. Individual is 2 years of age or older with moderate to severe PJIA; **AND**
   B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy [nonbiologic DMARDs (such as methotrexate)];

OR

VIII. Non-infectious uveitis (UV) when each of the following criteria are met (Levy-Clarke 2014):
   A. Individual has chronic, recurrent, treatment-refractory or vision-threatening disease; **AND**
   B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy [such as corticosteroids or immunosuppressants (azathioprine, cyclosporine, or methotrexate]);

OR

IX. Immune checkpoint inhibitor therapy-related toxicities [severe (grade 3) or life threatening (grade 4) adverse events) in an individual with any of the following conditions (NCCN 2A):
   A. Severe or life-threatening diarrhea or colitis unresponsive to high-dose systemic corticosteroids; **OR**
   B. Severe or life-threatening pneumonitis if no improvement after 48 hours of high-dose systemic corticosteroids; **OR**
   C. Severe or life-threatening renal failure or elevated serum creatinine (that is, greater than 3 times baseline or greater than 4.0 mg/dL) if toxicity remains greater than grade 2 after 1 week of corticosteroids; **OR**
   D. Severe or life-threatening cardiovascular adverse events (such as, arrhythmias, impaired ventricular function, myocarditis, or pericarditis); **OR**
   E. Severe or life-threatening inflammatory arthritis unresponsive to corticosteroids or anti-inflammatory agents;

OR

XI. Sarcoidosis when each of the following criteria are met (Baughman 2006):

Market Applicability						
Market	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	NA

A. Individual is 18 years of age or older; **AND**
B. Individual has chronic, progressive, treatment-refractory disease; **AND**
C. Individual has had an inadequate response to, is intolerant of, or has a contraindication to systemic corticosteroids; **AND**
D. Individual has had an inadequate response to, is intolerant of, or has a contraindication to nonbiologic DMARDs (such as methotrexate or azathioprine).

Requests for Avsola (infliximab-axxq), Inflectra (infliximab-dyyb), Remicade (infliximab), or Renflexis (infliximab-abda) may **not** be approved for the following:

I. All other indications not included above; **OR**
II. In combination with other TNF antagonists, apremilast, JAK inhibitors, or other biologic drugs (such as abatacept, anakinra, tocilizumab, or vedolizumab); **OR**
III. Tuberculosis, other active serious infections, or a history of recurrent infections; **OR**
IV. Individual has not had a tuberculin skin test (TST) or a Centers for Disease Control (CDC-) and Prevention -recommended equivalent to evaluate for latent tuberculosis prior to initiating infliximab.

Note:
TNFi have black box warnings for serious infections and malignancy. Individuals treated with TNFi are at increased risk for developing serious infections that may lead to hospitalization or death. Most individuals who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. TNFi should be discontinued if an individual develops a serious infection or sepsis. Individuals should be tested for latent tuberculosis (TB) before TNFi use and during therapy. Treatment for latent TB should be initiated prior to TNFi use. Risks and benefits of TNFi should be carefully considered prior to initiation of therapy in individuals with chronic or recurrent infection. Lymphoma and other malignancies have been reported in children and adolescents treated with TNFi. Postmarketing cases of hepatosplenic T-cell lymphoma (HSTCL) have been reported in individuals treated with TNFi. Almost all cases had received treatment with azathioprine or 6-mercaptopurine concomitantly with a TNFi at or prior to diagnosis. It is uncertain whether HSTCL is related to the use of a TNFi or a TNFi in combination with these other immunosuppressants.

Key References:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2018. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. Brunner HI, Ruperto N, Tzaribachev N, et al. Subcutaneous golimumab for children with active polyarticular-course juvenile idiopathic arthritis: results of a multicentre, double-blind, randomised-withdrawal trial. Ann Rheum Dis. 2018; 77(1):21-29.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: September 14, 2018.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2018; Updated periodically.

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Market Applicability						
Market	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	NA

6. NCCN Drugs & Biologics Compendium (NCCN Compendium®) 2016 National Comprehensive Cancer Network, Inc. Available at: NCCN.org. Updated periodically. Accessed on: September 14, 2018.
7. Singh JA, Saag KG, Bridges SL et al. 2015 American College of Rheumatology Guideline for the treatment of rheumatoid arthritis. Arthritis Rheum. 2016;68:1-26.
8. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol*. 2019; 80: 1029-72.
9. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. Arthritis Rheum. 2019; 71(1): 5-32.
10. American Gastroenterological Association. Identification, assessment and initial medical treatment of ulcerative colitis Clinical Care Pathway. Available at https://gastro.org/guidelines/ibd-and-bowel-disorders. Accessed on: September 14, 2018.
11. American Gastroenterological Association. Identification, assessment and initial medical treatment of Crohn's disease Clinical Care Pathway. Available at https://gastro.org/guidelines/ibd-and-bowel-disorders. Accessed on: September 14, 2018.
12. Lichtenstein GR, Loftus EV, Isaacs KL et al. 2018 American College of Gastroenterology Guideline for the management of Crohn's disease in adults. Am J Gastroenterol 2018; 113:481–517.
13. Rubin DT, Ananthakrishnan AN, Siegel CA et al. American College of Gastroenterology Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol 2019; 114:384-413.
14. Ward MM. Deodhar A, Gensler LS, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/ Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Rheumatol. 2019; 71(10):1599-1613.
15. Ringold S, Weiss PF, Beukelman T, et al. 2013 Update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. Arthritis Rheum. 2013; 65(10):2499-2512.
16. Ringold S, Angeles-Han ST, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. Arthritis Rheum. 2019; 71(6):846-863.
17. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care & Research. 2011; 63(4):465-482.
18. Levy-Clarke G, Jabs DA, Read RW, et al. Expert panel recommendations for the use of anti-tumor necrosis factor biologic agents in patients with ocular inflammatory disorders; American Uveitis Society subcommittee. Ophthalmology. 2014; 121(3):785-796.
19. Baughman RP, Drent M, et al. Infliximab therapy in patients with chronic sarcoidosis and pulmonary involvement. Am J Respir Crit Care Med. 2006; 174:795-802.
20. Lahdenne P, Vahasalo P, & Honkanen V: Infliximab or etanercept in the treatment of children with refractory juvenile idiopathic arthritis: an open label study. Ann Rheum Dis 2003; 62(3):245-247.
21. Gerloni V, Pontikaki I, Gattinara M, et al: Efficacy of repeated intravenous infusions of an anti-tumor necrosis factor alpha monoclonal antibody, infliximab, in persistently active, refractory juvenile idiopathic arthritis: results of an open-label prospective study. Arthritis Rheum 2005; 52(2):548-553.

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