

Infliximab (Remicade[®], Inflectra[®], Renflexis[®], Avsola[™])

When requesting an infliximab product (Remicade, Inflectra, Renflexis, Avsola) for non-oncology indications, the individual requiring treatment must be diagnosed with an FDA-approved indication or approved off-label compendial use and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-approved Indications

Infliximab is indicated for the treatment of:

- Crohn's disease
- Ulcerative colitis
- Rheumatoid arthritis
- Psoriatic arthritis
- Plaque psoriasis
- Ankylosing spondylitis

Approved Off-label Compendial Uses

- Behcet's disease
- Graft-versus-host disease
- Hidradenitis suppurativa
- Colitis, indeterminate
- Juvenile idiopathic arthritis
- Pyoderma gangrenosum
- Sarcoidosis
- Scleritis or sterile corneal ulceration
- Still's disease
- Spondyloarthritis, other subtypes
- Uveitis
- Immunotherapy-related toxicities associated with checkpoint inhibitor therapy

Coverage Guidelines

The individual must meet the following criteria for select indications:

Rheumatoid arthritis (RA)

Initial authorization:

- Had a 3-month trial of at least one biologic agent OR at least one conventional synthetic disease-modifying antirheumatic drug (DMARD); AND
- Infliximab is prescribed by or in consultation with a rheumatologist.

Ankylosing spondylitis (AS)

Initial authorization:

- Infliximab is prescribed by or in consultation with a rheumatologist.

Psoriatic arthritis (PsA)*Initial authorization:*

- Infliximab is prescribed by or in consultation with a rheumatologist or a dermatologist.

Crohn's disease (CD)*Initial authorization:*

- Meets one of the following conditions:
 - Has enterocutaneous (perianal or abdominal) or rectovaginal fistulas;
 - Had ileocolonic resection;
 - Has tried one other agent (e.g., certolizumab, adalimumab, vedolizumab, ustekinumab, methotrexate, 6-mercaptopurine,);
 - Has tried or is currently taking corticosteroids; OR
 - Has a contraindication to corticosteroid therapy; AND
- Is 6 years of age or older; AND
- Infliximab is prescribed by or in consultation with a gastroenterologist.

Ulcerative colitis (UC)*Initial authorization:*

- Has tried or had an intolerance to at least one systemic agent including a biologic (e.g., adalimumab, vedolizumab, 6-mercaptopurine, azathioprine); OR
- Has pouchitis and has tried at least one of the following therapies: antibiotic, probiotic, corticosteroid enema, or Rowasa (mesalamine) enema; AND
- Is 6 years of age or older; AND
- Infliximab is prescribed by or in consultation with a gastroenterologist.

Plaque psoriasis (PP)*Initial authorization:*

- Meets one of the following conditions:
 - Had a 3-month trial of or intolerance to at least one biologic agent;
 - Had a 3-month trial of or intolerance to at least one traditional systemic agent (e.g., methotrexate, cyclosporine, acitretin); OR
 - Has a contraindication to methotrexate therapy; AND
- Is 18 years of age or older; AND
- Infliximab is prescribed by or in consultation with a dermatologist.

Behcet's disease*Initial authorization:*

- Meets one of the following conditions:
 - Has ophthalmic manifestations of Behcet's disease;
 - Had a trial of at least one tumor necrosis factor (TNF) inhibitor (e.g., adalimumab, etanercept); OR
 - Has tried at least one conventional therapy (e.g., systemic corticosteroids, immunosuppressant, interferon alfa); AND
- Infliximab is prescribed by or in consultation with one of the following specialists: rheumatologist, dermatologist, ophthalmologist, gastroenterologist, or neurologist.

Graft-versus-host disease (GVHD)*Initial authorization:*

- Has tried at least one conventional systemic treatment for GVHD (e.g., cyclosporine, thalidomide, tacrolimus, mycophenolate mofetil, corticosteroids); AND
- Infliximab is prescribed by or in consultation with an oncologist, hematologist, or a physician affiliated with a transplant center.

Hidradenitis suppurativa*Initial authorization:*

- Has tried one other therapy (e.g., intralesional or oral corticosteroids, systemic antibiotics, isotretinoin); AND
- Infliximab is prescribed by or in consultation with a dermatologist.

Colitis, indeterminate*Initial authorization:*

- Has tried all of the following agents: one systemic corticosteroid, mesalamine, and azathioprine/6-mercaptopurine; AND
- Is 6 years of age or older; AND
- Infliximab is prescribed by or in consultation with a gastroenterologist.

Juvenile idiopathic arthritis*Initial authorization:*

- Has tried one other agent for this condition (e.g., adalimumab, etanercept, methotrexate, non-steroidal anti-inflammatory drug [NSAID]); OR
- Has aggressive disease; AND
- Infliximab is prescribed by or in consultation with a rheumatologist.

Pyoderma gangrenosum*Initial authorization:*

- Has tried one systemic corticosteroid; OR
- Had a 2-month trial of or intolerance to at least one immunosuppressive agent (e.g., mycophenolate, cyclosporine); AND
- Infliximab is prescribed by or in consultation with a dermatologist.

Sarcoidosis*Initial authorization:*

- Has tried at least one systemic corticosteroid; AND
- Has tried at least one immunosuppressive agent (e.g., methotrexate, azathioprine, cyclosporine); AND
- Infliximab is prescribed by or in consultation with a pulmonologist, ophthalmologist, or dermatologist.

Scleritis or sterile corneal ulceration*Initial authorization:*

- Has tried one other therapy for this condition (e.g., corticosteroid, methotrexate, cyclosporine, NSAID); AND
- Infliximab is prescribed by or in consultation with an ophthalmologist.

Still's disease

Initial authorization:

- Has tried one corticosteroid; AND
- Had a 2-month trial of or intolerance to at least one conventional synthetic DMARD (e.g., methotrexate); AND
- Infliximab is prescribed by or in consultation with a rheumatologist.

Spondyloarthritis (SpA), other subtypes

Initial authorization:

- Has axial spondyloarthritis and has objective signs of inflammation defined as one of the following:
 - C-reactive protein elevated beyond the upper limit of normal for the reporting laboratory; OR
 - Sacroiliitis reported on MRI; OR
- Has arthritis primarily in the knees, ankles, elbows, wrist, hands, and/or feet and has tried at least one conventional synthetic DMARD (e.g., methotrexate, leflunomide); AND
- Infliximab is prescribed by or in consultation with a rheumatologist.

Uveitis

Initial authorization:

- Had a trial of either an etanercept product (e.g., Enbrel) or an adalimumab product (e.g., Humira); OR
- Has tried periocular/intraocular/systemic corticosteroids or immunosuppressive agent; AND
- Infliximab is prescribed by or in consultation with an ophthalmologist.

Immunotherapy-related toxicities associated with checkpoint inhibitor therapy

Initial authorization:

- Developed an immunotherapy-related toxicity involving the gastrointestinal system, inflammatory arthritis, or ocular toxicity; AND
- Developed the immune-related toxicity while receiving a checkpoint inhibitor (e.g., Keytruda, Opdivo, Yervoy, Tecentriq, Bavancio, Imfinzi); AND
- Has tried a systemic corticosteroid (e.g., methylprednisolone, prednisone); AND
- Infliximab is prescribed by or in consultation with an oncologist, gastroenterologist, rheumatologist, or ophthalmologist.

For reauthorization (for all indications):

The individual must have responded to infliximab therapy for reauthorization.

Approval duration (initial):

- GVHD: 1 month
- Colitis, indeterminate or pyoderma gangrenosum: 4 months
- All others: 3 months

Approval duration (renewal):

- GVHD: 3 months
- All others: 12 months

Dosing Recommendations

Infliximab is administered by intravenous infusion over a period of not less than 2 hours.

Crohn's disease, ulcerative colitis, indeterminate colitis, plaque psoriasis, psoriatic arthritis, hidradenitis suppurativa, and pyoderma gangrenosum

Approve initial therapy up to 5 mg/kg at 0, 2 and 6 weeks, then no more frequently than once every 8 weeks. Patients currently receiving infliximab may receive approval up to a maximum dose of 10 mg/kg administered no more frequently than once every 4 weeks.

Graft-versus-host disease

Approve up to a maximum dose of 10 mg/kg administered no more frequently than once weekly.

Rheumatoid arthritis

Approve initial therapy up to 3 mg/kg at 0, 2 and 6 weeks, then no more frequently than once every 8 weeks. Patients currently receiving infliximab may receive approval up to a maximum dose of 10 mg/kg administered no more frequently than once every 4 weeks.

Ankylosing spondylitis, Behcet's disease, sarcoidosis, and spondyloarthritis

Approve initial therapy up to 5 mg/kg at 0, 2 and 6 weeks, then no more frequently than once every 6 weeks. Patients currently receiving infliximab may receive approval up to a maximum dose of 10 mg/kg administered no more frequently than once every 4 weeks.

Uveitis and immunotherapy-related toxicities associated with checkpoint inhibitor therapy

Approve initial therapy up to 10 mg/kg at 0, 2 and 6 weeks, then no more frequently than once every 4 weeks. Patients currently receiving infliximab may receive approval up to a maximum dose of 10 mg/kg administered no more frequently than once every 4 weeks.

Juvenile idiopathic arthritis and Still's disease

Approve initial therapy up to 6 mg/kg at 0, 2 and 6 weeks, then no more frequently than once every 8 weeks. Patients currently receiving infliximab may receive approval up to a maximum dose of 10 mg/kg administered no more frequently than once every 4 weeks.

Scleritis or sterile corneal ulceration

Approve initial therapy up to 10 mg/kg at baseline followed by up to three additional doses (for example, given 2, 6 and 8 weeks after the initial infusion). Patients currently receiving infliximab may receive approval up to a maximum dose of 10 mg/kg administered no more frequently than once every 4 weeks.

References

1. Remicade® injection [prescribing information]. Horsham, PA: Janssen Biotech; June 2018.
2. Inflectra™ injection for IV use [prescribing information]. Lake Forest, IL: Hospira/Pfizer; April 2016.
3. Renflexis injection for IV use [prescribing information]. Whitehouse Station, NJ: Samsung Bioepis/Merck; April 2017.
4. 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;(10):1599-1613.
5. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol*. 2018;113(4):481-517.
6. 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(4):1029-1072.
7. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis. *Arthritis Care Res (Hoboken)*. 2019;71(1):2-29.
8. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol*. 2016;68(1):1-26.
9. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol*. 2019;114(3):384-413.
10. Pardi DS, D'Haens G, Shen B, et al. Clinical guidelines for the management of pouchitis. *Inflamm Bowel Dis*. 2009;15(9):1424-1431.
11. Feuerstein JD, Isaac s KL, Schneider Y, et al. AGA clinical practice guidelines on the management of moderate to severe ulcerative colitis. *Gastroenterology*. 2020;158:1450-1461.
12. Hatemi G, Christensen R, Bang D, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. *Ann Rheum Dis*. 2018;77(6):808-818.
13. 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. *Ophthalmology*. 2014;121(3):785-796.
14. The NCCN/ASCO Management of Immunotherapy-Related Toxicities (Immune Checkpoint Inhibitor-Related Toxicities) Clinical Practice Guidelines in Oncology (Version 1.2020 – December 16, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed September 18, 2020.
15. 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 Rheumatol*. 2019;71(6):846-863.
16. 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.
17. Dabade TS, Davis MD. Diagnosis and treatment of the neutrophilic dermatoses (pyoderma gangrenosum, Sweet's syndrome). *Dermatol Ther*. 2011;24(2):273-284.
18. Amin EN, Closser DR, Crouser ED. Current best practice in the management of pulmonary and systemic sarcoidosis. *Ther Adv Respir Dis*. 2014;8(4):111-132.
19. The NCCN Hematopoietic Cell Transplantation (HCT): pre-transplant recipient evaluation and management of graft versus host disease Clinical Practice Guidelines in Oncology (Version 2.2020 – March 23, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on September 18, 2020.
20. Grant A, Gonzalez T, Montgomery MO, et al. Infliximab therapy for patients with moderate to severe hidradenitis suppurativa: a randomized, double-blind, placebo-controlled crossover trial. *J Am Acad Dermatol*. 2010;62(2):205-217.
21. Sullivan TP, Welsh E, Kerdell FA, et al. Infliximab for hidradenitis suppurativa. *Br J Dermatol*. 2003;149:1046-1049.
22. Fardet L, Dupuy A, Kerob D, et al. Infliximab for severe hidradenitis suppurativa: transient clinical efficacy in 7 consecutive patients. *J Am Acad Dermatol*. 2007;56:624-628.
23. Haslund P, Lee RA, Jemec GB. Treatment of hidradenitis suppurativa with tumour necrosis factor-alpha inhibitors. *Acta Derm Venereol*. 2009;89(6):595-600.
24. Papadakis KA, Treyzon L, Abreu MT, et al. Infliximab in the treatment of medically refractory indeterminate colitis. *Aliment Pharmacol Ther*. 2003;18:741-747.
25. Gornet JM, Couve S, Hassani Z, et al. Infliximab for refractory ulcerative colitis or indeterminate colitis: an open-label multicentre study. *Aliment Pharmacol Ther*. 2003;18:175-181.
26. Riera E, Olivé A, Narváez J, et al. Adult onset Still's disease: review of 41 cases. *Clin Exp Rheumatol*. 2011;29(2):331-336.
27. Pouchot J, Arlet JB. Biological treatment in adult-onset Still's disease. *Best Pract Res Clin Rheumatol*. 2012;26(4):477-487.
28. Kontzias A, Efthimiou P. Adult-onset Still's disease: pathogenesis, clinical manifestations and therapeutic advances. *Drugs*. 2008;68:319-337.

29. Furst DE, Keystone EC, So AK, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2012. *Ann Rheum Dis*. 2013;72 Suppl 2:ii2-34.
30. Xeljanz® tablets [prescribing information]. New York, NY: Pfizer Inc; February 2016.
31. Dastmalchi, M, Grundtman, C, Alexanderson, H, et al. A high incidence of disease flares in an open pilot study of infliximab in patients with refractory inflammatory myopathies. *Ann Rheum Dis*. 2008;67:1670-1677.
32. Mukhtyar C, Guillevin L, Cid MC, et al. EULAR recommendations for the management of large vessel vasculitis. *Ann Rheum Dis*. 2009;68(3):318-323.
33. Osman M, Pagnoux C, Dryden DM, et al. The role of biological agents in the management of large vessel vasculitis (LVV): a systematic review and meta-analysis. *PLoS One*. 2014 Dec 17;9(12):e115026.
34. Christophi GP, Ciorba MA. Lower Dose Infliximab for Ulcerative Colitis: How Low Can We Go and How Much Can be Saved? *J Clin Gastroenterol*. 2015;49(7):539-540.
35. Tayer-Shifman OE, Ilan O, Tovi H, Tal Y. Cogan's Syndrome – Clinical Guidelines and Novel Therapeutic Approaches. *Clin Rev Allergy Immunol*. 2014;47(1):65-72.
36. Hoffman GS, Merkel PA, Brasington RD, et al. Anti-tumor necrosis factor therapy in patients with difficult to treat Takayasu arteritis. *Arthritis Rheum*. 2004;50:2296-2304.
37. Mekinian A, Néel A, Sibilia J, et al. Efficacy and tolerance of infliximab in refractory Takayasu arteritis: French multicentre study. *Rheumatology (Oxford)*. 2012;51(5):882-886.
38. Buonuono PS, Bracaglia C, Campana A, et al. Infliximab therapy in pediatric Takayasu's arteritis: report of two cases. *Rheumatol Int*. 2011;31(1):93-95.
39. Molloy ES, Langford CA, Clark TM, et al. Anti-tumor necrosis factor therapy in patients with refractory Takayasu's arteritis: long-term follow-up. *Ann Rheum Dis*. 2008;67(11):1567-1569.
40. Schmidt J, Kermani TA, Bacani AK, et al. Tumor necrosis factor inhibitors in patients with Takayasu arteritis: experience from a referral center with long-term followup. *Arthritis Care Res (Hoboken)*. 2012;64(7):1079-1083.
41. Keystone EC. The utility of tumour necrosis factor blockade in orphan diseases. *Ann Rheum Dis*. 2004;63(Suppl 2):ii79-ii83.
42. Lamprecht P, Voswinkel J, Lilienthal T, et al. Effectiveness of TNF-alpha blockade with infliximab in refractory Wegener's granulomatosis. *Rheumatology (Oxford)*. 2002;41:1303-1307.
43. Booth A, Harper L, Hammad T, et al. Prospective study of TNF-alpha blockade with infliximab in anti-neutrophil cytoplasmic antibody-associated systemic vasculitis. *J Am Soc Nephrol*. 2004;15:717-721.
44. Samuels J, Spiera R. Newer therapeutic approaches to the vasculitides: biologic agents. *Rheum Dis Clin North Am*. 2006;32:187-200.
45. Bartolucci P, Ramanoelina J, Cohen P, et al. Efficacy of the anti-TNF-alpha antibody infliximab against refractory systemic vasculitides: an open pilot study on 10 patients. *Rheumatology (Oxford)*. 2002;41:1126-1132.
46. Salvarani C, Macchioni P, Manzini C, et al. Infliximab plus prednisone or placebo plus prednisone for the initial treatment of polymyalgia rheumatica: a randomized trial. *Ann Intern Med*. 2007;146:631-639.
47. Luqmani R. Treatment of polymyalgia rheumatica and giant cell arteritis: are we any further forward? *Ann Intern Med*. 2007;146:674-676.