Inflectra (infliximab-dyyb)
Remicade (infliximab)
Renflexis (infliximab-abda)
Effective January 1, 2020

Plan	☐ MassHealth ☒Commercial/Exchange	**Program Type**	☒ Prior Authorization ☐ Quantity Limit ☐ Step Therapy
Benefit	☒ Pharmacy Benefit ☒ Medical Benefit (NLX)		
Specialty Limitations	This medication has been designated specialty and must be filled at a contracted specialty pharmacy when obtained through the pharmacy benefit.		
Contact Information	**Specialty Medications**		
	All Plans	Phone: 866-814-5506	Fax: 866-249-6155
	Non-Specialty Medications		
	MassHealth	Phone: 877-433-7643	Fax: 866-255-7569
	Commercial	Phone: 800-294-5979	Fax: 888-836-0730
	Exchange	Phone: 855-582-2022	Fax: 855-245-2134
	Medical Specialty Medications (NLX)		
	All Plans	Phone: 844-345-2803	Fax: 844-851-0882
Exceptions	N/A		

Overview

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met, and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Moderately to severely active Crohn's disease
2. Moderately to severely active Ulcerative colitis
3. Moderately to severely active Rheumatoid arthritis in combination with methotrexate
4. Active Ankylosing spondylitis
5. Active Psoriatic arthritis
6. Chronic severe Plaque psoriasis

Compendial Uses

1. Axial spondyloarthritis
2. Behcet's syndrome
3. Granulomatosis with polyangiitis (Wegener's granulomatosis)
4. Hidradenitis suppurativa
5. Juvenile idiopathic arthritis
6. Pyoderma gangrenosum
7. Sarcoidosis
8. Takayasu's arteritis
9. Uveitis

All other indications are considered experimental/investigational and are not a covered benefit.

Coverage Guidelines

Moderately to severely active Crohn's disease (CD)

1. Authorization may be granted for members who are currently receiving treatment with Remicade, Inflectra, or Renflexis, excluding when the product is obtained as samples or via manufacturer's patient assistance programs.
   OR
2. Authorization may be granted for treatment of moderately to severely active CD when both of the following criteria are met:
   a. Member has an inadequate response, intolerance or contraindication to Humira (adalimumab)
   b. One of the following:
      - Member has fistulizing disease.
      - Member has an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix A).

Moderately to severely active ulcerative colitis (UC)

1. Authorization may be granted for members who are currently receiving treatment with Remicade, Inflectra, or Renflexis, excluding when the product is obtained as samples or via manufacturer's patient assistance programs.
   OR
2. Authorization may be granted for treatment of moderately to severely active UC when the member has an inadequate response, intolerance or contraindication to BOTH of the following:
   a. Humira (adalimumab)
   b. At least ONE conventional therapy option (see Appendix B).

Moderately to severely active rheumatoid arthritis (RA)

1. Authorization may be granted for members who are currently receiving treatment with Remicade, Inflectra, or Renflexis, excluding when the product is obtained as samples or via manufacturer's patient assistance programs.
   OR
2. Authorization may be granted for treatment of moderately to severely active RA when one of the following criteria is met:
   a. Member has experienced an inadequate response or intolerance to all preferred products (Enbrel, Humira and Rinvoq)
   b. Member has a contraindication to all preferred products (Enbrel, Humira and Rinvoq) and meets one of the following:
      - Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
      - Member has an intolerance or contraindication to methotrexate (see Appendix C).

Active ankylosing spondylitis (AS) and axial spondyloarthritis

1. Authorization may be granted for members who are currently receiving treatment with Remicade, Inflectra, or Renflexis, excluding when the product is obtained as samples or via manufacturer's patient assistance programs.
   OR
2. Authorization may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when any of the following criteria is met:
   a. One of the following:
      - Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs) for at least four weeks.
      - Member has an intolerance or contraindication to two or more NSAIDs.

      AND
   b. For members with ankylosing spondylitis, member has had a documented inadequate response or intolerable adverse event with ALL the preferred products: Humira, Enbrel and Cosentyx or member has a documented clinical reason to avoid these products.

Active psoriatic arthritis (PsA)

1. Authorization may be granted for members who are currently receiving treatment with Remicade, Inflectra, or Renflexis, excluding when the product is obtained as samples or via manufacturer's patient assistance programs.
   OR
2. Authorization may be granted for treatment of active psoriatic arthritis (PsA) if any of the following criteria is met:
   a. Member has had a documented inadequate response or intolerable adverse event with ALL the preferred products (Cosentyx, Enbrel, Humira, Otezla and Stelara).
   b. Member has a contraindication to all the preferred products AND meets one of the following:
      - Patient has had an intolerance to or inadequate response (after at least 3 months of treatment) with methotrexate OR leflunomide.
      - Patient has a contraindication to BOTH methotrexate and leflunomide AND has experienced an inadequate response, intolerance, or contraindication to sulfasalazine.

Chronic severe plaque psoriasis

1. Authorization may be granted for members who are currently receiving treatment with Remicade, Inflectra, or Renflexis, excluding when the product is obtained as samples or via manufacturer's patient assistance programs.
   OR
2. Authorization may be granted for treatment of chronic severe plaque psoriasis when all the following criteria are met:
   a. Member has had a documented inadequate response or intolerable adverse event with ALL the preferred products (Cosentyx, Enbrel, Humira, Otezla, Skyrizi and Stelara) unless there is a documented clinical reason to avoid these products.
   b. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   c. Member meets any of the following criteria:
      - Member has experienced an inadequate response or adverse reaction to TWO conventional therapies in any one of the following combinations:

- 1 topical agent + 1 systemic agent (methotrexate, acitretin or cyclosporine)
- 1 topical agent + 1 phototherapy (e.g., UVB, PUVA)
- 1 systemic agent + 1 phototherapy (e.g., UVB, PUVA)
- 2 systemic agents

- Member has a clinical reason to avoid ALL conventional therapies (topical agents, phototherapy and systemic agents). See Appendix C.
- Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

Behcet's syndrome
Authorization may be granted for treatment of refractory Behcet's syndrome

Granulomatosis with polyangiitis (Wegener's granulomatosis)
Authorization may be granted for treatment of granulomatosis with polyangiitis

Hidradenitis suppurativa
Authorization may be granted for treatment of severe, refractory hidradenitis suppurativa when documentation of Hurley stage III HS received.

Juvenile Idiopathic arthritis (JIA)
1. Authorization may be granted for members who have previously received Remicade, Inflectra, or Renflexis.
   OR
2. Authorization may be granted for treatment of JIA when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least a 3-month trial of a self-injectable TNF inhibitor indicated for JIA (e.g., Enbrel or Humira).
   a. Member has experienced an intolerable adverse event (e.g., hypersensitivity reaction) to a self-injectable TNF inhibitor indicated for JIA.
   b. Member has developed antibodies against Enbrel or Humira.

Pyoderma gangrenosum
Authorization may be granted for treatment of pyoderma gangrenosum.

Sarcoidosis
Authorization may be granted for treatment of refractory sarcoidosis

M. Takayasu's arteritis
Authorization may be granted for treatment of Takayasu's arteritis.

N. Uveitis
Authorization may be granted for treatment of uveitis in members who have experienced an inadequate response or intolerance or have a contraindication to a trial of immunosuppressive therapy for uveitis (e.g., methotrexate, azathioprine, or mycophenolate mofetil).

Continuation of Therapy

Authorization may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Remicade, Inflectra or Renflexis as evidenced by low disease activity or improvement in signs and symptoms of the condition.

Limitations

1. Approvals will be granted for 24 months
2. For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).
    a. Note: Members who have received Inflectra, Remicade, Renflexis, or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.
3. The following quantity limits apply:

Remicade 100 mg	10 vials per 28 days

Appendices

Appendix A
Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
    a. Oral mesalamine
2. Mild to moderate disease – maintenance of remission:
    a. Azathioprine, mercaptopurine
    b. Alternatives: methotrexate intramuscularly (IM)
3. Moderate to severe disease – induction of remission:
    a. Methotrexate IM
4. Moderate to severe disease – maintenance of remission:
    a. Azathioprine, mercaptopurine
    b. Alternative: methotrexate IM
5. Perianal and fistulizing disease – maintenance of remission
    a. Azathioprine, mercaptopurine
    b. Alternative: methotrexate IM

Appendix B
Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
    a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa)
    b. Rectal mesalamine (e.g., Canasa, Rowasa)
    c. Alternatives: azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
    a. Oral mesalamine, rectal mesalamine
    b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission:
    a. Sulfasalazine
4. Severe disease – maintenance of remission:
    a. Azathioprine, mercaptopurine
    b. Alternative: sulfasalazine
    c. Pouchitis: rectal mesalamine

Appendix C
Examples of Clinical Reasons (Contraindications) to Avoid Pharmacologic Treatment with Methotrexate, Acitretin or Cyclosporine

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction
12. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

References

1. Remicade (infliximab) [prescribing information]. Horsham, PA: Janssen Biotech, Inc; June 2018.
2. Renflexis (infliximab) [prescribing information]. Whitehouse Station, NJ: Merck Sharp & Dohme; November 2017.
3. Inflectra (infliximab dyyb) [prescribing information]. New York, NY: Pfizer; November 2017
4. Yoo DH, Racewicz A, Brzezicki J, et al. A phase III randomized study to evaluate the efficacy and safety of CT-P13 compared with reference infliximab in patients with active rheumatoid arthritis: 54-week results from the PLANETRA study. *Arthritis Res Ther*. 2016;18:82.[PubMed 27038608]
5. Park W, Yoo DH, Jaworski J, et al. Comparable long-term efficacy, as assessed by patient-reported outcomes, safety and pharmacokinetics, of CT-P13 and reference infliximab in patients with ankylosing spondylitis: 54-week results from the randomized, parallel-group PLANETAS study. *Arthritis Res Ther*. 2016;18:25.[PubMed 26795209]
6. van der Heijde D, Ramiro S, Landewe R, et al. 2016 Update of the international ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis.* 2017;0:1-14.
7. Meyer A, Rudant J, Drouin J, et al. Effectiveness and Safety of Reference Infliximab and Biosimilar in Crohn Disease: A French Equivalence Study. Ann Intern Med 2019; 170:99.
8. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum.* 2008;59(6):762-784.
9. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017*;0*:1-18.
10. 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.
11. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.

12. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies; 2015 update. *Ann Rheum Dis*. 2016;75(3):499-510.
13. Peluso R, Lervolino S, Vitiello M, et al. Extra-articular manifestations in psoriatic arthritis patients. Clin Rheumatol. 2014 May 8. [Epub ahead of print].
14. 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 & Rheumatism.* 2013;65:2499-2512.
15. Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol.* 2015: 10.1002/art.39298. [Epub ahead of print].
16. Baughman RP, Lower EE. Infliximab for refractory sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis 2001; 18:70
17. Della Rossa A, Tavoni A, Merlini G, et al. Two Takayasu arteritis patients successfully treated with infliximab: a potential disease-modifying agent? Rheumatology (Oxford) 2005; 44:1074
18. Mooij JE, van Rappard DC, Mekkes JR. Six patients with pyoderma gangrenosum successfully treated with infliximab. Int J Dermatol 2013; 52:1418
19. Tugal-Tutkun I, Mudun A, Urgancioglu M, et al. Efficacy of infliximab in the treatment of uveitis that is resistant to treatment with the combination of azathioprine, cyclosporine, and corticosteroids in Behçet's disease: an open-label trial. Arthritis Rheum 2005; 52:2478
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; 62:205
Laharie D, Bourreille A, Branche J, et al. Long-term outcome of patients with steroid-refractory acute severe UC treated with ciclosporin or infliximab. Gut 2017

Review History

03/21/05 – Reviewed
05/15/05 – Implemented
02/27/06 – Updated
02/25/08 – Updated
02/23/09 – Updated
02/22/10 – Reviewed
02/28/11 – Updated
02/27/12 – Updated
02/25/13 – Updated
02/24/14 – Updated
02/23/15 – Reviewed
02/22/16 – Reviewed
02/27/17 - Added Inflectra; adopted SGM & PDS
02/26/18 – Updated
02/20/19 – Updated
11/20/19 - Added all SGM compendial uses that were previously listed on custom criteria as reviewed on a case-by-case basis and deleted off-label case-by-case reviews statement. Added criteria to compendial

diagnosis. Added Skyrizi as required preferred product for PsO. Added Rinvoq as required preferred trial for RA

Disclaimer

AllWays Health Partners complies with applicable federal civil rights laws and does not discriminate or exclude people on the basis of race, color, national origin age, disability, or sex.