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## Overview

This document addresses the use of tumor necrosis factor inhibitors (TNFi) which target specific pathways of the immune system and either enhance or inhibit the immune response. Indications are drug-specific but TNFi are approved for the treatment of rheumatoid arthritis, psoriasis, psoriatic arthritis, Crohn's disease, ulcerative colitis, ankylosing spondylitis, juvenile idiopathic arthritis, hidradenitis suppurativa, non-infectious uveitis, and other conditions as applicable. Agents addressed in this document include:

- Adalimumab agents (Humira, Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, Hyrimoz)
- Certolizumab pegol (Cimzia)
- Etanercept agents (Enbrel, Erelzi, Eticovo)
- Golimumab (Simponi, Simponi Aria)
- Infliximab agents (Remicade, Infliximab, Avsola, Inflectra, Ixifi, Renflexis)

**Rheumatoid Arthritis:** The American College of Rheumatology (ACR) guidelines recommend disease-modifying antirheumatic drug (DMARD) monotherapy as first-line treatment in individuals with RA with moderate to high disease activity. Methotrexate (MTX) monotherapy, titrated to a dose of at least 15 mg, is recommended over hydroxychloroquine, sulfasalazine, and leflunomide. Methotrexate monotherapy is also recommended over monotherapy with biologics (TNFi, IL-6 inhibitors, abatacept) or JAK inhibitors. For individuals taking maximally tolerated doses MTX who are not at target, the addition of a biologic or JAK inhibitor is recommended. Non-TNFi biologics or JAK inhibitors are conditionally recommended over TNFi in individuals with heart failure.

**Plaque Psoriasis (otherwise known as psoriasis vulgaris):** The American Academy of Dermatology (AAD) and National Psoriasis Foundation (NPF) published joint guidelines on the management and treatment of psoriasis with biologics. The guidelines do not include a treatment algorithm or compare biologics to each other or conventional therapy. The guideline notes that patients with mild-moderate disease may be adequately controlled with topical therapy and/or phototherapy while moderate to severe disease may necessitate treatment with a biologic. Moderate to severe disease is defined as involvement in > 3% of body surface area (BSA) or involvement in sensitive areas that significantly impact daily function (such as palms, soles of feet, head/neck, or genitalia). TNFi biologics, ustekinumab, IL17 inhibitors, and IL23 inhibitors are all recommended as monotherapy treatment options for adult patients with moderate to severe plaque psoriasis. Combination use of TNFi biologics (etanercept, infliximab, adalimumab) and ustekinumab with apremilast is poorly studied and the AAD has given this practice a grade C recommendation based on limited-quality evidence.

**Psoriatic Arthritis:** The American College of Rheumatology (ACR) guidelines recommend that initial treatment of patients with active severe PsA or concomitant psoriasis should include a TNFi biologic over an oral small molecule (OSM; including methotrexate, sulfasalazine, cyclosporine, leflunomide, and apremilast). For initial therapy, OSMs are preferred over IL-17 and ustekinumab; and may be considered over TNFi biologics in mild to moderate disease without comorbid conditions or in those who prefer oral therapy. Recommendations involving biologics over OSMs as first line therapy are conditional and based on low quality evidence. Evidence cited includes indirect comparisons of placebo-controlled trials, studies with open-label design, and extrapolation from studies in plaque psoriasis. Furthermore, most pivotal trials for TNFi biologics included a study population that were DMARD experienced. Overall, there is a lack of definitive evidence for the safety and efficacy of biologic drugs over conventional therapy for the initial treatment of most patients with psoriatic arthritis. The ACR guidelines also include recommendations for patients whose disease remains active despite treatment with an OSM. Here, TNFi biologics are recommended over other therapies including IL-17 inhibitors, ustekinumab, tofacitinib, and abatacept. When TNFi biologics are not used, IL-17 inhibitors are preferred over ustekinumab; both of which are preferred over tofacitinib and abatacept. For disease that remains active despite TNFi monotherapy, switching to a different TNFi is recommended over other therapies.

**Crohn's Disease:** According to the American Gastrointestinal Association clinical practice guidelines, evidence supports the use of methotrexate, corticosteroids, TNFi +/- immunomodulator, ustekinumab, or vedolizumab for induction of remission. Among the biologics, infliximab, adalimumab, ustekinumab, or vedolizumab are recommended or suggested over certolizumab for induction of remission. Evidence supports biologic agents, thiopurines, and methotrexate for maintenance of remission. Ustekinumab and vedolizumab are options for individuals with primary nonresponse to initial treatment with TNFi. Adalimumab, ustekinumab, or vedolizumab may be used in cases where an individual previously responded to infliximab and then lost response (secondary nonresponse).

**Ulcerative Colitis:** For those with moderately to severely active disease, the American College of Gastroenterology (ACG) guidelines strongly recommend induction of remission using oral budesonide MMX, oral systemic corticosteroids, TNFi, tofacitinib or vedolizumab (moderate to high quality evidence). The American Gastroenterological Association (AGA) guidelines define moderate to severe UC as those who are dependent on or refractory to corticosteroids, have severe endoscopic disease activity, or are at high risk of colectomy. AGA strongly recommends biologics (TNFi, vedolizumab, or ustekinumab) or tofacitinib over no treatment in induction and maintenance of remission (moderate quality of evidence). For biologic-naïve individuals, Infliximab or vedolizumab are conditionally recommended over adalimumab for induction of remission (moderate quality evidence).

**Axial Spondyloarthritis:** Spondyloarthritis with predominantly axial involvement includes both ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA), based upon the presence or absence, respectively, of abnormalities of the sacroiliac joints on plain radiography. The American College of Rheumatology (ACR) and Spondylitis Association of America guidance recommend NSAIDs as initial treatment for AS and nr-axSpA. In adults with active AS despite treatment with NSAIDs, DMARDs [including sulfasalazine or MTX], TNF inhibitors, and IL-17 inhibitors [secukinumab or ixekizumab] are recommended. TNFi treatment is recommended over IL-17 inhibitors. IL-17 inhibitors are recommended over a different TNFi in patients with primary nonresponse to TNFi (no initial response). An alternative TNFi is recommended in patients with secondary nonresponse to the first TNFi used (relapse after initial response). Recommendations for nr-axSpA are largely extrapolated from evidence in AS; only certolizumab has been approved for this indication.

**Juvenile Idiopathic Arthritis:** The American College of Rheumatology (ACR) guidelines provide recommendations for juvenile idiopathic arthritis, including systemic disease (SJIA) and JIA with polyarthritis (PJIA). SJIA is an autoinflammatory condition marked by intermittent fever, rash, and arthritis. PJIA is marked by the presence of more than four affected joints in the first six months of illness. For children with active systemic features and varying degrees of synovitis, therapy with IL-1 inhibitors (anakinra or canakinumab) or tocilizumab may be considered after initial therapy with NSAIDs or corticosteroids. For children without active systemic features and varying degrees of synovitis, anakinra or tocilizumab may be considered after initial therapy with DMARDs (methotrexate or leflunomide). TNFi or abatacept may be considered if polyarthritis is present (ACR 2013). For children with active polyarthritis, biologic therapy including TNFi, abatacept, or tocilizumab +/- DMARD is recommended following initial DMARD therapy (preferably methotrexate) (ACR 2019).

**Other uses:** The National Comprehensive Cancer Network® (NCCN) provides recommendations for off-label use of etanercept and adalimumab with a category 2A level of evidence. These include the use of etanercept in steroid-refractory graft versus host disease and the use of etanercept or adalimumab for immune checkpoint Inhibitor-related inflammatory arthritis. High-quality evidence supporting its safety and efficacy in these conditions has not been reported.

**Biosimilar and Interchangeable Agents:** Biosimilar products must be highly similar to the reference product and there must be no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product. Biosimilars must utilize the same mechanism of action (MOA), route of administration, dosage form and strength as the reference product; and the indications proposed must have been previously approved for the reference product. The potential exists for a biosimilar product to be approved for one or more indications for which the reference product is licensed based on extrapolation of data intended to demonstrate biosimilarity in one indication. Sufficient scientific justification for extrapolating data is necessary for FDA approval. Factors and issues that should be considered for extrapolation include the MOA for each indication, the pharmacokinetics, bio-distribution, and immunogenicity of the product in different patient populations, and differences in expected toxicities in each indication and patient population. As biosimilar agents must demonstrate similarity to the reference product in FDA indications, it is reasonable that biosimilarity can be extrapolated to off-label indications as well. In contrast to biosimilar status, an interchangeable biologic must meet the biosimilar standards, but also must be expected to produce the same clinical result as the reference product in any given patient; and if administered more than once to a patient, the risk in terms of safety or diminished efficacy from altering or switching between use of the reference or interchangeable product is not greater than that from use of the reference product without such alteration or switch.

There are currently four FDA approved infliximab biosimilar agents, Inflectra (infliximab-dyyb), Ixifi (infliximab-qbtx), Renflexis (infliximab-abda), and Avsola (infliximab-axxq). There is also one FDA approved unbranded product called Infliximab. Infliximab is the same product as Remicade and has the same label, but was approved as an unbranded biologic, not a generic or biosimilar. All four biosimilar products share the same FDA approved indications as Remicade and, as biosimilars, are dosed and administered the same way. The approval of each agent was based on pharmacokinetic data, clinical comparative efficacy data, and extrapolation to selected indications of the reference product. In a randomized, double-blind, non-inferiority trial, adults with RA, ankylosing spondyloarthritis, psoriatic arthritis, Crohn's disease, ulcerative colitis, and psoriasis on stable treatment with reference products were randomized to continue reference product or switch to Inflectra at the same dose for 52 weeks. The primary endpoint, disease worsening, occurred in 26.2% and 29.6% of patients in the reference and biosimilar groups, respectively, demonstrating non-inferiority within the pre-specified margin of 15%. The frequency of adverse events was similar between groups (Jorgensen 2017). In a phase 3, double-blind, active-controlled study, individuals with RA randomized to Ixifi or reference product were re-randomized to continue on reference or switch to

the biosimilar at week 30. Authors concluded that at week 54, the efficacy, safety, and immunogenicity were similar between groups and not affected by treatment switching (Alten 2019). Another randomized, double-blind, non-inferiority trial in adults with RA randomized individuals to continue reference product or switch to Renflexis at the same dosing schedule for 24 weeks. Response rate by ACR20 was 68.8% and 63.5% in reference and biosimilar groups, respectively, after transition period. Authors concluded that no clinically meaningful difference in terms of efficacy, safety, and immunogenicity was observed in the switch group compared to the reference group (Smolen 2018). A randomized, double-blind, active-controlled, comparative clinical study supports a single switch from Remicade to Avsola in 556 patients with Rheumatoid Arthritis (RA). Avsola was non-inferior to Remicade (given at the same dose and schedule) when both were given for 52 weeks as measured by ACR20. The authors concluded that this study demonstrated the safety and immunogenicity of Avsola were similar to those of the reference product and that the efficacy and safety were not impacted by a single switch from infliximab reference to Avsola (Genovese 2020).

There are five FDA approved adalimumab biosimilar products: Abrilada (adalimumab-afzb); Amjevita (adalimumab-atto); Hyrimoz (adalimumab-adaz); Hadlima (adalimumab-bwvd), and Hulio (adalimumab-fkjp). These products share the same FDA approved indications as Humira, with the exception of hidradenitis suppurativa, uveitis, and select pediatric approvals. As biosimilars, these products are dosed and administered the same way, though equivalent dosage strengths are not available for all products currently. The approval of each agent was based on pharmacokinetic data, clinical comparative efficacy data, and extrapolation to selected indications of the reference product. There is also evidence supporting at least a single switch between reference product and biosimilar in select indications. These studies indicate that a single switch does not result in considerable alterations in efficacy, safety, and immunogenicity of the product (Cohen 2019, Fleischmann 2021, Blauvelt 2021, Wiland 2021, Weinblatt 2018, Genovese 2020, Papp 2017). There is one FDA approved interchangeable adalimumab product: Cyltezo (adalimumab-adbm). Supportive studies for Cyltezo include phase 3 randomized, double blind studies in patients with Crohn's Disease (Hanauer 2021), Psoriasis (Menter 2020), and Rheumatoid Arthritis (Cohen 2018). Interchangeability of Cyltezo has been demonstrated for the conditions of use, strengths, dosage forms, and route of administration described in its prescribing information. As an interchangeable product, Cyltezo can be expected to produce the same clinical result as the reference product in any given patient; and if administered more than one to a patient, the risk in terms of safety or diminished efficacy from alternating or switching between the use of the reference product or Cyltezo is not greater than that from the reference product without such alternation or switch.

Tumor necrosis factor inhibitors 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.

Use of TNFi has been associated with rare cases of new onset or exacerbation of demyelinating disease including multiple sclerosis and Guillain-Barre syndrome. Exercise caution if considering the use of TNFi in individuals with preexisting or recent-onset central or peripheral nervous system demyelinating disorders and discontinuation should be considered if any of these disorders develop.

Cases of worsening congestive heart failure (CHF) and new onset CHF have been reported with TNFi. TNFi should be used with caution in CHF and individuals should be monitored closely. The clinician should consider the status of an individual with moderate or severe heart failure (New York Heart Association (NYHA) Functional Class III-IV) before initiating treatment with infliximab at doses greater than 5mg/kg.

## Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

### Cimzia (certolizumab pegol)

Initial requests for Cimzia (certolizumab pegol) may be approved for the following:

- I. Crohn's disease (CD) when each of the following criteria are met:
  - A. Individual is 18 years of age or older with 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 systemic corticosteroids or immunosuppressants);
- OR**
- II. 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 methotrexate titrated to maximally tolerated dose (ACR 2021); **OR**

- C. If methotrexate is not tolerated or contraindicated, individual has had an inadequate response to, is intolerant of, or has a contraindication to other conventional therapy (sulfasalazine, leflunomide, or hydroxychloroquine);

**OR**

III. 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 DMARDs (such as sulfasalazine)];

**OR**

IV. Non-radiographic axial spondyloarthritis (nr-axSpA) when each of the following criteria are met:

- A. Individual is 18 years of age or older with moderate to severe nr-axSpA; **AND**
- B. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy [such as NSAIDs or nonbiologic 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 DMARDs (such as methotrexate, sulfasalazine, or leflunomide)];

**OR**

VI. Plaque psoriasis (Ps) 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 with either of the following (AAD 2019):
  - 1. Plaque Ps involving greater than three percent (3%) body surface area (BSA); **OR**
  - 2. Plaque Ps 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 therapy (such as acitretin, cyclosporine, or methotrexate).

Continuation requests for Cimzia (certolizumab pegol) may be approved if the following criterion is met:

- I. There is confirmation of clinically significant improvement or stabilization in clinical signs and symptoms of the disease.

Requests for Cimzia (certolizumab pegol) 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, ozanimod, or other biologic drugs (such as, abatacept, anakinra, IL-17 inhibitors, IL-23 inhibitors, ustekinumab, tocilizumab, rituximab, or vedolizumab); **OR**
- III. Tuberculosis, other active serious infections, or a history of recurrent infections; **OR**
- IV. If initiating therapy, 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 (unless switching therapy from another targeted immune modulator and no new risk factors).

### **Enbrel (etanercept); Erelzi (etanercept-szzs); Eticovo (etanercept-ykro)**

Initial requests for Enbrel (etanercept), Erelzi (etanercept-szzs), or Eticovo (etanercept-ykro) may be approved for the following:

- I. 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 methotrexate titrated to maximally tolerated dose (ACR 2021); **OR**
  - C. If methotrexate is not tolerated or contraindicated, individual has had an inadequate response to, is intolerant of, or has a contraindication to other conventional therapy (sulfasalazine, leflunomide, or hydroxychloroquine);

**OR**

II. 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 DMARDs (such as sulfasalazine)] (ACR 2019);

**OR**

III. Polyarticular juvenile idiopathic arthritis (PJIA) when each of the following criteria are met:

- 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)] (ACR 2019);

**OR**

IV. 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 DMARDs (such as methotrexate, sulfasalazine, or leflunomide)];

**OR**

V. Plaque psoriasis (Ps) when each of the following criteria are met:

- A. Individual is 4 years of age or older with chronic moderate to severe (that is, extensive or disabling) plaque Ps with either of the following (AAD 2019):
  - 1. Plaque Ps involving greater than three percent (3%) body surface area (BSA); **OR**

2. Plaque Ps 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 therapy (such as acitretin, cyclosporine, or methotrexate).

Continuation requests for Enbrel (etanercept), Erelzi (etanercept-szszs), or Eticovo (etanercept-ykro) may be approved if the following criterion is met:

- I. There is confirmation of clinically significant improvement or stabilization in clinical signs and symptoms of the disease.

Requests for Enbrel (etanercept), Erelzi (etanercept-szszs), or Eticovo (entanercept-ykro) 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, ozanimod, other biologic drugs (such as, abatacept, anakinra, IL-17 inhibitors, IL-23 inhibitors, rituximab, tocilizumab, ustekinumab, vedolizumab), or cyclophosphamides; **OR**
- III. Tuberculosis, other active serious infections, or a history of recurrent infections; **OR**
- IV. If initiating therapy, 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 (unless switching therapy from another targeted immune modulator and no new risk factors).

**Humira (adalimumab); Abrilada (adalimumab-afzb); Amjevita (adalimumab-atto); Cyltezo (adalimumab-adbm); Hadlima (adalimumab-bwwd); Hulio (adalimumab-fkjp); Hyrimoz (adalimumab-adaz);**

Initial requests for Humira (adalimumab), Abrilada (adalimumab-afzb), Amjevita (adalimumab-atto), Cyltezo (adalimumab-adbm), Hadlima (adalimumab-bwwd), Hulio (adalimumab-fkjp), or Hyrimoz (adalimumab-adaz), or may be approved for the following:

- I. Crohn's disease (CD) when each of the following criteria are met:
  - A. Individual is 6 years of age or older with 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 systemic corticosteroids or immunosuppressants);
- OR**
- II. Ulcerative colitis (UC) when each of the following criteria are met:
  - A. Individual is 5 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 methotrexate titrated to maximally tolerated dose (ACR 2021); **OR**
  - C. If methotrexate is not tolerated or contraindicated, individual has had an inadequate response to, is intolerant of, or has a contraindication to other conventional therapy (sulfasalazine, leflunomide, or hydroxychloroquine);
- 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 DMARDs (such as sulfasalazine)];
- OR**
- V. Polyarticular juvenile idiopathic arthritis (PJIA) when each of the following criteria are met:
  - 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)] (ACR 2019);
- OR**
- VI. 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 DMARDs (such as methotrexate, sulfasalazine, or leflunomide)];
- OR**
- VII. Plaque psoriasis (Ps) 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 with either of the following (AAD 2019):
    1. Plaque Ps involving greater than three percent (3%) body surface area (BSA); **OR**
    2. Plaque Ps 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 therapy (such as acitretin, cyclosporine, or methotrexate);
- OR**
- VIII. Non-infectious uveitis (UV) when each of the following criteria are met:
  - 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. Hidradenitis suppurativa (HS) when each of the following criteria are met:

- A. Individual is 12 years of age or older; **AND**
- B. Individual has moderate to severe HS (Hurley stage II or Hurley stage III disease); **AND**
- C. Individual has had an inadequate response to, is intolerant of, or has a contraindication to conventional therapy (such as oral antibiotics);

**OR**

X. Sarcoidosis when each of the following criteria are met (Sweiss 2014):

- 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).

Continuation requests for Humira (adalimumab), Abrilada (adalimumab-afzb), Amjevita (adalimumab-atto), Cyltezo (adalimumab-adbm), Hadlima (adalimumab-bwwd), Hulio (adalimumab-fkjp), Hyrimoz (adalimumab-adaz), or may be approved if the following criterion is met:

- I. There is confirmation of clinically significant improvement or stabilization in clinical signs and symptoms of the disease.

Requests for Humira (adalimumab), Abrilada (adalimumab-afzb), Amjevita (adalimumab-atto), Cyltezo (adalimumab-adbm), Hadlima (adalimumab-bwwd), Hyrimoz (adalimumab-adaz), or Hulio (adalimumab-fkjp) 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, ozanimod, or other biologic drugs (such as abatacept, anakinra, IL-17 inhibitors, IL-23 inhibitors, ustekinumab, rituximab, tocilizumab, or vedolizumab); **OR**
- III. Tuberculosis, other active serious infections, or a history of recurrent infections; **OR**
- IV. If initiating therapy, 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 (unless switching therapy from another targeted immune modulator and no new risk factors).

**Remicade (infliximab); Avsola (infliximab-axxq); Inflectra (infliximab-dyyb); Infliximab (unbranded); Ixifi (infliximab-qbtx), Renflexis (infliximab-adba)**

Requests for Remicade (infliximab), Avsola (infliximab-axxq), Inflectra (infliximab-dyyb), Infliximab (unbranded); Ixifi (infliximab-qbtx), or Renflexis (infliximab-adba) may be approved for the following:

- I. Crohn's disease (CD) when each of the following criteria are met:
  - A. Individual is 6 years of age or older with 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 systemic corticosteroids or immunosuppressants);**OR**
  - C. Individual is 6 years of age or older with fistulizing CD;

**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 methotrexate titrated to maximally tolerated dose (ACR 2021); **OR**
- C. If methotrexate is not tolerated or contraindicated, individual has had an inadequate response to, is intolerant of, or has a contraindication to other conventional therapy (sulfasalazine, leflunomide, or hydroxychloroquine);

**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 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 DMARDs (such as methotrexate, sulfasalazine, or leflunomide)];

**OR**

VI. Plaque psoriasis (Ps) 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 with either of the following (AAD 2019):
  - 1. Plaque Ps involving greater than three percent (3%) body surface area (BSA); **OR**
  - 2. Plaque Ps 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 therapy (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**
- F. Severe or life-threatening steroid-refractory myalgias or myositis;

**OR**

X. Sarcoidosis when each of the following criteria are met (Sweiss 2014):

- 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).

Continuation requests for Remicade (infliximab), Avsola (infliximab-axxq), Inflectra (infliximab-dyyb), Infliximab (unbranded); Ixifi (infliximab-qbtx), or Renflexis (infliximab-adba) may be approved if the following criterion is met:

- I. There is confirmation of clinically significant improvement or stabilization in clinical signs and symptoms of the disease.

Requests for Remicade (infliximab), Avsola (infliximab-axxq), Inflectra (infliximab-dyyb), Infliximab (unbranded); Ixifi (infliximab-qbtx), or Renflexis (infliximab-adba) 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, ozanimod, or other biologic drugs (such as, abatacept, anakinra, IL-17 inhibitors, IL-23 inhibitors, rituximab, ustekinumab, tocilizumab, or vedolizumab); **OR**
- III. Tuberculosis, other active serious infections, or a history of recurrent infections; **OR**
- IV. If initiating therapy, 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 (unless switching therapy from another targeted immune modulator and no new risk factors).

### Simponi, Simponi Aria (golimumab)

Initial requests for Simponi (golimumab) may be approved for the following:

- I. Ulcerative colitis (UC) when each of the following criteria are met:
  - A. Individual is 18 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**

II. 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 DMARDs (such as sulfasalazine)];

**OR**

III. 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 DMARDs (such as methotrexate, sulfasalazine, or leflunomide)];

- OR**
- IV. 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 methotrexate titrated to maximally tolerated dose (ACR 2021); **OR**
    - C. If methotrexate is not tolerated or contraindicated, individual has had an inadequate response to, is intolerant of, or has a contraindication to other conventional therapy (sulfasalazine, leflunomide, or hydroxychloroquine).

Initial requests for Simponi Aria (golimumab) may be approved if the following criteria are met:

- I. 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 DMARDs (such as sulfasalazine)];

- OR**
- II. Psoriatic arthritis (PsA) when each of the following criteria are met:
    - A. Individual is 2 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 DMARDs (such as methotrexate, sulfasalazine, or leflunomide)];

- 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 methotrexate titrated to maximally tolerated dose (ACR 2021); **OR**
    - C. If methotrexate is not tolerated or contraindicated, individual has had an inadequate response to, is intolerant of, or has a contraindication to other conventional therapy (sulfasalazine, leflunomide, or hydroxychloroquine).

- OR**
- IV. Polyarticular juvenile idiopathic arthritis (PJIA) when each of the following criteria are met:
    - 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)] (ACR 2019).

Continuation requests for Simponi and Simponi Aria (golimumab) may be approved if the following criterion is met:

- I. There is confirmation of clinically significant improvement or stabilization in clinical signs and symptoms of the disease.

Requests for Simponi and Simponi Aria (golimumab) 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, ozanimod, or other biologic drugs (such as, abatacept, anakinra, IL-17 inhibitors, IL-23 inhibitors, rituximab, tocilizumab, ustekinumab, or vedolizumab); **OR**
- III. Tuberculosis, other active serious infections, or a history of recurrent infections; **OR**
- IV. If initiating therapy, 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 (unless switching therapy from another targeted immune modulator and no new risk factors).

## Step Therapy

**Note:** When a tumor necrosis factor antagonist is deemed approvable based on the clinical criteria above, the benefit plan may have additional criteria requiring the use of a preferred<sup>1</sup> agent or agents.

### Infliximab Agents Step Therapy

A list of the preferred tumor necrosis factor antagonist(s) is available [here](#).

Requests for a non-preferred infliximab reference agent (Remicade) or corresponding unbranded Infliximab or biosimilar agent (Avsola, Inflectra, Renflexis) may be approved when the following criteria are met:

- I. Individual has had a trial and intolerance to one preferred agent;

- OR**
- II. Individual has been receiving the requested non-preferred agent; **AND**
  - III. Individual has previously undergone at least one switch between infliximab agents (reference or biosimilar agents);

**OR**



#In the treatment of Rheumatoid Arthritis (RA): May approve up to 4 (four) syringes, autoinjectors, or pens (40mg) [up to an additional 2 (two) syringes, autoinjectors, or pens] every 28 days if the individual is unable to take concomitant methotrexate.

\*Initiation of therapy for adult Crohn's Disease (CD) or Ulcerative Colitis (UC) or Hidradenitis Suppurativa (HS): May approve 1 (one) Crohn's Disease/Ulcerative Colitis/Hidradenitis Suppurativa starter pack OR up to 4 (four) additional 40 mg pens or syringes OR up to a total of 3 (three) 80 mg pens in the first month (28 days) of treatment.

^Initiation of therapy for Plaque Psoriasis (Ps): May approve 1 (one) Psoriasis starter pack OR up to 2 (two) additional 40 mg pens, autoinjectors, or syringes OR up to 1 (one) 80 mg pen in the first month (28 days) of treatment.

§ Maintenance therapy for Hidradenitis Suppurativa (HS): May approve up to 2 (two) additional 40 mg pens or syringes per each 28 days.

@ Initiation of therapy for adolescent Hidradenitis Suppurativa (HS): Depending on individual's weight, may approve one (1) adolescent or adult Hidradenitis Suppurativa starter pack OR up to 4 (four) additional 40 mg pens or syringes ~~(40 mg)~~ OR up to a total of 3 (three) 80 mg pens in the first month (28 days) of treatment.

†Initiation of therapy for pediatric Crohn's Disease (CD): Depending on individual's weight, may approve one (1) pediatric or adult Crohn's Disease starter pack OR up to 4 (four) additional 40 mg pens or syringes OR up to a total of 3 (three) 80 mg pens in the first month (28 days) of treatment.

‡Initiation of therapy for Uveitis (UV): May approve 1 (one) Uveitis starter pack OR up to 2 (two) additional 40 mg pens, autoinjectors, or syringes in the first month (28 days) of treatment.

\*In the treatment of Ulcerative Colitis (UC): May approve up to 4 (four) syringes, autoinjectors, or pens (40mg) [up to an additional 2 (two) syringes, autoinjectors, or pens] every 28 days for individuals 5-17 years of age weighing at least 40 kg (88 lbs)<sup>Δ</sup>. May approve up to 4 (four) syringes, autoinjectors, or pens (20mg) [up to an additional 2 (two) syringes, autoinjectors, or pens] every 28 days for individuals 5-17 years of age weighing 20 kg (44 lbs) to 40 kg (88 lbs)<sup>Δ</sup>.

◊Initiation of therapy for pediatric Ulcerative Colitis (UC): Depending on individual's weight, may approve one (1) pediatric Ulcerative Colitis starter pack OR up to 5 (five) additional 40 mg pens or syringes OR up to a total of 4 (four) 80 mg pens in the first month (28 days) of treatment.

⊞Requests for 80mg/ 0.8 mL pen for maintenance dosing require clinical review. Initial requests for maintenance treatment of up to 2 pens per 28 days may be approved if the following criteria are met<sup>Δ</sup>:

- I. Individual has a diagnosis of Rheumatoid Arthritis (RA); **AND**
- II. Individual is unable to take concomitant methotrexate;  
**OR**
- III. Individual has a diagnosis of Hidradenitis Suppurativa (HS);  
**OR**
- IV. Individual has a diagnosis of Ulcerative Colitis (UC); **AND**
- V. Individual is 5 to 17 years of age; **AND**
- VI. Individual weighs at least 40 kg (88 lbs).

<sup>Δ</sup>Individuals with UC who are well controlled on 20 to 40 mg every week or 80 mg every other week regimen may continue therapy.

## Etanercept Agents Quantity Limits

Drug	Limit
Erelzi (etanercept-szszs) 25 mg/0.5 mL prefilled syringe*	8 syringes per 28 days
Erelzi (etanercept-szszs) 50 mg/0.5 mL prefilled syringe*, Sensoready® pen*	4 syringes/pens per 28 days
Enbrel (etanercept) 25 mg/mL vial*	8 vials per 28 days
Enbrel (etanercept) 25 mg/0.5 mL (0.51 mL) prefilled syringe*	8 syringes per 28 days
Enbrel (etanercept) 50 mg/mL (0.98 mL) prefilled syringe*, SureClick® autoinjector*	4 syringes/autoinjectors per 28 days
Enbrel (etanercept) 50 mg/mL Mini™ prefilled cartridge with AutoTouch™*	4 cartridges per 28 days
Eticovo (etanercept-ykro) 25 mg/0.5 mL prefilled syringe*	8 syringes per 28 days
Eticovo (etanercept-ykro) 50 mg/mL prefilled syringe*	4 syringes per 28 days
Override Criteria	
*Initiation of therapy for adult Plaque Psoriasis (Ps): May approve up to 2 (two) additional 25 mg vials (25 mg/mL) or syringes [(25 mg/0.5 mL (0.51 mL))] OR 1 (one) additional 50 mg syringe [50 mg/mL (0.98 mL)], pen (50 mg/0.5 mL), autoinjector [50 mg/mL (0.98 mL)], or cartridge (50 mg/mL) per week in the first 3 months (84 days) of treatment.	

## Infliximab Quantity Limit

Drug	Limit
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Remicade (infliximab) 100 mg vial	5 mg/kg as frequently as every 8 weeks
Avsola (infliximab-axxq) 100 mg vial	5 mg/kg as frequently as every 8 weeks
Renflexis (infliximab-abda) 100 mg vial	5 mg/kg as frequently as every 8 weeks
Inflectra (infliximab-dyyb) 100 mg vial	5 mg/kg as frequently as every 8 weeks
Infliximab 100 mg vial	5 mg/kg as frequently as every 8 weeks
Ixifi (infliximab-qbtx) 100 mg vial	5 mg/kg as frequently as every 8 weeks
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), may approve 5 mg/kg as frequent as every 6 weeks.
III.	For Rheumatoid Arthritis (RA), may approve dose escalation up to 10 mg/kg every 8 weeks OR 3 mg/kg every 4 weeks for individuals who have an incomplete response.
IV.	For Crohn's Disease (CD), may approve dose escalation up to 10 mg/kg every 8 weeks if the individual has previously achieved response to infliximab at standard dosing and subsequently lost response.

### Simponi (golimumab) Quantity Limits

Drug	Limit
Simponi (golimumab) 50 mg/0.5 mL SmartJect® autoinjector	1 autoinjector per 28 days
Simponi (golimumab) 50 mg/0.5 mL prefilled syringe	1 syringe per 28 days
Simponi (golimumab) 100 mg/1 mL SmartJect® autoinjector*	1 autoinjector per 28 days
Simponi (golimumab) 100 mg/1 mL prefilled syringe*	1 syringe per 28 days
Override Criteria	
*Initiation of therapy for Ulcerative Colitis (UC): May approve up to 2 (two) additional syringes or autoinjectors (100 mg/1 mL) in the first month (28 days) of treatment.	

### Simponi Aria (golimumab) Quantity Limit

Drug	Limit
Simponi Aria (golimumab) 50 mg vial	2 mg/kg as frequently as every 8 weeks
Override Criteria	
*For initiation of therapy, may approve up to 2 mg/kg (or 80 mg/m <sup>2</sup> for individuals <18 years of age) at weeks 0 and 4	

## Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

### HCPCS

<b>C9399</b>	Unclassified drugs or biologicals [when specified as adalimumab-afzb (Abrilada)]
<b>J0135</b>	Injection, adalimumab, 20 mg [Humira]
<b>J0717</b>	Injection, certolizumab pegol, 1 mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self-administered) [Cimzia]
<b>J1438</b>	Injection, etanercept; 25 mg (when drug administered under the direct supervision of a physician, not for use when drug is self-administered) [Enbrel]
<b>J1602</b>	Injection, golimumab, 1 mg, for intravenous use [Simponi Aria]
<b>J1745</b>	Injection, infliximab, excludes biosimilar, 5 mg [Remicade]
<b>Q5121</b>	Injection, infliximab-axxq, biosimilar, (Avsola), 10 mg
<b>J3590</b>	Unclassified biologics [no specific code for golimumab (Simponi), etanercept-szsz (Erelzi), adalimumab-atto (Amjevita), adalimumab-adbm (Cyltezo), adalimumab-adaz (Hyrimoz), etanercept-ykro (Etivoco), adalimumab-bwwd (Hadlima), adalimumab-afzb (Abrilada), Hulio (adalimumab-fkjp)]
<b>Q5103</b>	Injection, infliximab-dyyb, biosimilar, (Inflectra), 10 mg
<b>Q5104</b>	Injection, infliximab-abda, biosimilar, (Renflexis), 10 mg
<b>Q5109</b>	Injection, infliximab-qbtx, biosimilar, (Ixifi), 5 mg
<b>S9359</b>	Home infusion therapy, antitumor necrosis factor intravenous therapy; (e.g., Infliximab); per diem

ICD-10 Diagnosis

<b>D86.0-D86.9</b>	Sarcoidosis [Remicade, Inflectra, Renflexis, Ixifi; Humira, Cyltezo]
<b>H20.00-H20.9</b>	Iridocyclitis [Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Cyltezo]
<b>H44.111-H44.119</b>	Panuveitis [Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Cyltezo]
<b>H44.131-H44.139</b>	Sympathetic uveitis [Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Cyltezo]
<b>I30.8</b>	Other forms of acute pericarditis [Remicade, Inflectra, Renflexis, Ixifi]
<b>I30.9</b>	Acute pericarditis, unspecified [Remicade, Inflectra, Renflexis, Ixifi]
<b>I40.8</b>	Other acute myocarditis [Remicade, Inflectra, Renflexis, Ixifi]
<b>I40.9</b>	Acute myocarditis, unspecified [Remicade, Inflectra, Renflexis, Ixifi]
<b>I50.9</b>	Heart failure, unspecified [Remicade, Inflectra, Renflexis, Ixifi]
<b>J70.2</b>	Acute drug-induced interstitial lung disorders [Remicade, Inflectra, Renflexis, Ixifi]
<b>J70.4</b>	Drug-induced interstitial lung disorders, unspecified [Remicade, Inflectra, Renflexis, Ixifi]
<b>K50.00-K50.919</b>	Crohn's disease (regional enteritis) [Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Hadlima, Cyltezo; Cimzia]
<b>K51.00-K51.919</b>	Ulcerative colitis [Enbrel, Erelzi; Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Hadlima, Cyltezo; Simponi]
<b>K52.1</b>	Toxic gastroenteritis and colitis [Remicade, Inflectra, Renflexis, Ixifi]
<b>K60.4</b>	Rectal fistula [Remicade, Inflectra, Renflexis, Ixifi]
<b>L40.0</b>	Psoriasis vulgaris (plaque psoriasis) [Enbrel, Erelzi, Eticovo; Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Cyltezo; Cimzia]
<b>L40.1</b>	Generalized pustular psoriasis [Enbrel, Erelz, Eticovpi; Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Hadlima, Cyltezo; Cimzia]
<b>L40.2</b>	Acrodermatitis continua [Enbrel, Erelzi, Eticovo; Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Cyltezo; Cimzia]
<b>L40.3</b>	Pustulosis palmaris et plantaris [Enbrel, Erelzi, Eticovo; Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Hadlima, Cyltezo; Cimzia]
<b>L40.4</b>	Guttate psoriasis [Enbrel, Erelzi, Eticovo; Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Hadlima Cyltezo; Cimzia]
<b>L40.50-L40.59</b>	Arthropathic psoriasis [Enbrel, Erelzi, Eticovo; Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Cyltezo; Simponi; Simponi Aria; Cimzia]
<b>L40.8-L40.9</b>	Psoriasis, other and unspecified [Enbrel, Erelzi, Eticovo; Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Hadlima, Cyltezo; Cimzia]
<b>L73.2</b>	Hidradenitis suppurativa [Humira, Amjevita, Hadlima, Cyltezo]
<b>M05.00-M05.9</b>	Rheumatoid arthritis with rheumatoid factor [Enbrel, Erelzi, Eticovo; Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Hadlima, Cyltezo; Cimzia; Simponi; Simponi Aria]
<b>M06.00-M06.09</b>	Rheumatoid arthritis without rheumatoid factor [Enbrel, Erelzi, Eticovo; Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Hadlima, Cyltezo; Cimzia; Simponi; Simponi Aria]
<b>M06.4</b>	Inflammatory polyarthropathy [Remicade, Inflectra, Renflexis, Ixifi]
<b>M06.80-M06.89</b>	Other specified rheumatoid arthritis [Enbrel, Erelzi, Eticovo; Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Hadlima, Cyltezo; Cimzia; Simponi; Simponi Aria]
<b>M06.9</b>	Rheumatoid arthritis, unspecified [Enbrel, Erelzi, Eticovo; Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Hadlima, Cyltezo; Cimzia; Simponi; Simponi Aria]
<b>M08.00-M08.09</b>	Unspecified juvenile rheumatoid arthritis [Enbrel, Erelzi, Eticovo; Humira, Amjevita, Hadlima Cyltezo; Remicade, Inflectra, Renflexis, Ixifi]
<b>M08.20-M08.29</b>	Juvenile rheumatoid arthritis with systemic onset [Enbrel, Erelzi, Eticovo; Humira, Amjevita, Hadlima Cyltezo; Remicade, Inflectra, Renflexis, Ixifi]
<b>M08.3</b>	Juvenile rheumatoid polyarthritis (seronegative) [Enbrel, Erelzi, Eticovo; Humira, Amjevita, Hadlima Cyltezo; Remicade, Inflectra, Renflexis, Ixifi]
<b>M08.40-M08.48</b>	Pauciarticular juvenile rheumatoid arthritis [Enbrel, Erelzi, Eticovo; Humira, Amjevita, Hadlima, Cyltezo; Remicade, Inflectra, Renflexis, Ixifi]
<b>M08.80-M08.99</b>	Other or unspecified juvenile arthritis [Enbrel, Erelzi, Eticovo; Humira, Amjevita, Hadlima, Cyltezo; Remicade, Inflectra, Renflexis, Ixifi]
<b>M35.2</b>	Behçet's disease [related uveitis; Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Hadlima, Cyltezo]
<b>M45.0-M45.9</b>	Ankylosing spondylitis [Enbrel, Erelzi, Eticovo; Remicade, Inflectra, Renflexis, Ixifi; Humira, Amjevita, Hadlima, Cyltezo; Simponi; Simponi Aria; Cimzia]
<b>M46.81</b>	Other specified inflammatory spondylopathies, occipito-atlanto-axial region
<b>M47.9</b>	Spondylosis, unspecified
<b>N17.8</b>	Other acute kidney failure [Remicade, Inflectra, Renflexis, Ixifi]

<b>N17.9</b>	Acute kidney failure, unspecified [Remicade, Inflectra, Renflexis, Ixifi]
<b>N82.3</b>	Fistula of vagina to large intestine (rectovaginal fistula) [Remicade, Inflectra, Renflexis, Ixifi]
<b>R19.7</b>	Diarrhea, unspecified [Remicade, Inflectra, Renflexis, Ixifi]

## Document History

Revised: 11/19/2021

Document History:

- 12/20/2021 – Step therapy table update.
- 11/19/2021 – Annual Review: Update rheumatoid arthritis criteria to align with guidelines and emphasize methotrexate; create new adalimumab biosimilar and interchangeable step therapy; add new biosimilars Hulio and Ixifi and unbranded biologic Infliximab to criteria, step therapy, and quantity limits; update infliximab criteria for immunotherapy-related toxicities per NCCN; update and align exclusion list for combination use; clarify TB testing language; clarify which overrides apply to which dosage forms for adalimumab quantity limits; create overrides for adolescent HS and pediatric UC; allow 80 mg pen to be used for initiation of therapy where applicable; Coding Reviewed: Added Hulio to J3590.
- 08/20/2021 – Select Review: Update infliximab step therapy to allow pediatric individuals with UC or CD to continue on current non-preferred agent. Coding reviewed: No changes.
- 05/21/2021 – Select Review: Update Humira clinical criteria to include new pediatric indication for ulcerative colitis; clarify may not be approved section; add quantity limit for Humira 80 mg dosage form and pediatric UC starter pack per label; add additional quantity limit overrides as needed. Update to step therapy table. Coding Reviewed: No changes.
- 05/11/2021 – Update to step therapy table.
- 11/20/2020 – Annual Review: Add continuation of use criteria; remove 5-ASA as conventional therapy in CD; update tuberculosis testing language; update golimumab prior authorization and quantity limit as applicable with new indication for polyarticular juvenile idiopathic arthritis and pediatric psoriatic arthritis; update infliximab criteria to allow fistulizing CD without failure of conventional therapy; update infliximab quantity limit to 5 mg/kg and update overrides according to FDA label; update adalimumab quantity limit to remove override for escalated dosing in IBD. Coding Reviewed: No changes.
- 02/21/2020 – Select Review: Add new biosimilars Avsola and Abrilada to prior authorizations and quantity limits; add Avsola as potential preferred to infliximab step therapy per designation. Coding Reviewed: Added HCPCS C9399. Added Avsola and Abrilada to J3590. Coding Review 5/15/2020: Medicare update. 6/1/2020 Added ICD-10-CM M46.81 Added HCPCS Q5121 for Avsola, (Effective 7/1/2020), Deleted Avsola from J3590.
- 11/15/2019 – Annual Review: Update definition of moderate psoriasis using BSA based on guidelines; add new biosimilars Eticovo and Hadlima to prior authorizations and quantity limits; add quantity limit for new Cyltezo dosage form; update references; wording and formatting updates. Coding Reviewed: Added Hadlima and Eticovo to J3590 and applicable ICD10 codes.
- 09/23/2019 - Administrative update to add drug specific quantity limit.
- 05/17/2019 – Select Review: Add new non-radiographic axial spondyloarthritis indication to Cimzia criteria and reference new indication in quantity limit. Add ICD-10 M47.9. Coding Reviewed: Added ICD-10dx M46.81 Other specified inflammatory spondylopathies, occipito-atlanto-axial region
- 02/22/2019 – Select Review: Add new off-label indication for refractory sarcoidosis in infliximab agents and adalimumab agents clinical criteria. Add new ST for Infliximab Reference and Biosimilar Agents. Coding Update: Add D86.0-D86.9 to reflect addition of refractory sarcoidosis indication.
- 11/16/2018 – Annual Review: Initial P&T review of Tumor Necrosis Factor Antagonists Clinical Guideline. Update clinical criteria to delete “active” disease wording. Update criteria to delete requirement agent is being used “to reduce signs and symptoms, maintain clinical response”, etc. Add biosimilar agents (Amjevita, Cyltezo, Hyrimoz, Erelzi, Inflectra, Renflexis) to applicable approval criteria. Delete requirement for methotrexate combination therapy for RA indication in infliximab and golimumab approval criteria for consistency with other TNF agents and in accordance with ACR guideline recommendations. Lower age requirement to 12 for hidradenitis suppurativa in adalimumab criteria with expanded approval in adolescents. Add examples of conventional therapy to approval criteria for clarity. Update certolizumab QL override criteria to add new psoriasis indication. Add new QL for Hyrimoz. Wording and formatting changes to criteria for consistency. HCPCS Coding Review: no change. HCPCS Coding Review: add Q5109 for Ixifi and revised J3590 description effective 1/1/2019. No ICD-10 coding changes.

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### ING-CC-0062 Tumor Necrosis Factor Antagonists

#### Commercial Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
06/01/2017 to 06/30/2021	Remicade	Avsola Inflectra Renflexis
07/01/2021	Inflectra Remicade, infliximab (unbranded)	Avsola Renflexis
01/01/2021 CalPERS For members 18 years and older, step therapy criteria applies to new starts only (defined as no use of Remicade in the last 12 months)	Avsola Inflectra Renflexis	Remicade

#### Medicaid Medical Benefit

Effective Date	Preferred Agents	Non-Preferred Agents
11/01/2020 - AR, NV, NY, VA, WI		
1/1/2021 - CA, GA, IN, KY, MD, NJ, SC, TN, WNY	Avsola	Remicade Inflectra Renflexis
2/1/2021 - LA		

5/1/2021 – IA		
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**Medicare Medical Benefit**

<b>Effective Date</b>	<b>Preferred Agents</b>	<b>Non-Preferred Agents</b>
07/15/2021	Inflectra Remicade	Avsola Renflexis