Definition: Humira is a recombinant human immunoglobulin G1 (IgG1) monoclonal antibody specific for human tumor necrosis factor alpha (TNFα). It neutralizes the biological activity of TNFα and inhibits binding of TNFα with its receptors. TNF, a naturally occurring cytokine, mediates inflammation and modulates cellular immune responses. Increased levels of TNF are found in the synovial fluid of patients with rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS). TNF has an important role in both the pathologic inflammation and the joint destruction that are characteristic of these diseases. Increased levels of TNF are found in psoriasis plaques but the mechanism of action in plaque psoriasis and Crohn’s disease are not known.

Boxed Warnings
Humira has boxed warnings concerning risks of serious infection and the risk of malignancy. Prior to initiating therapy with Humira, patients should be evaluated for active tuberculosis (TB) infection; periodically during therapy, patients should be assessed for latent TB infection. Patients should also be monitored for signs and symptoms of infection during and after treatment with Humira, and if a serious infection or sepsis develops, Humira should be discontinued. It is also recommended that patients treated with any TNF antagonist should be monitored for malignancies.

Recommended Authorization Criteria
Coverage of Humira is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

1. Rheumatoid Arthritis (RA) in an Adult
   a) Initial Therapy. Approve for 3 months if the patient meets BOTH of the following criteria (i and ii):
      i. The patient meets ONE of the following conditions (1, 2, 3, or 4):
         1. Patient has tried one DMARD (brand or generic; oral or injectable) for at least 3 months, [this includes patients who have tried other biologic DMARDs for at least 3 months]; OR
         2. Patient is concurrently receiving MTX; OR
         3. Patient has a contraindication or intolerance to MTX and leflunomide, as determined by the prescribing physician (This criterion is recommended based on the professional opinion of specialized physicians.); OR
         4. Patient has early RA (defined as disease duration of < 6 months) with at least one of the following features of poor prognosis: functional limitation
(e.g., based on Health Assessment Questionnaire Disability Index [HAQ-DI] score); extraarticular disease such as rheumatoid nodules, RA vasculitis, or Felty’s syndrome; positive rheumatoid factor or anti-cyclic citrullinated protein (anti-CCP) antibodies; or bony erosions by radiograph; AND

ii. Humira is prescribed by or in consultation with a rheumatologist.

b) Patients Currently Receiving Humira. Approve for 1 year if the patient has had a response (e.g., less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improved laboratory values; reduced dosage of corticosteroids), as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Humira.

Humira is indicated for moderate or severe active RA in adults and can be used alone or in combination with MTX or other DMARDs. Most patients will have received initial therapy with MTX, another oral DMARD(s) (e.g., hydroxychloroquine, leflunomide, sulfasalazine, MTX), or combination DMARD therapy (including double or triple therapy). However, current recommendations from the American College of Rheumatology (ACR) [2012] note that patients with early RA (defined as disease duration < 6 months) with important markers of poor prognosis may be started early on a biologic agent such as Humira, either alone or in combination with MTX. The guidelines generally recommend assessment at Month 3 with a general recommendation to switch biologic in patients with a loss or lack of benefit at this assessment. The criteria for patients with contraindications or intolerance to DMARDs are recommended based on the professional opinion of specialized physicians.

**Dosing in RA.** Dosage and administration consistent with U.S. Food and Drug Administration approved label (i.e., 40 mg every other week. Dosing frequency may be increased to 40 mg every week)

2. **Ankylosing Spondylitis (AS)**

a) **Initial Therapy.** Approve for 3 months if prescribed by or in consultation with a rheumatologist.

b) **Patients Currently Receiving Humira.** Approve for 1 year if the patient has had a response (e.g., decreased pain or stiffness, improved function or activities of daily living), as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Humira.

Humira is indicated for ankylosing spondylitis. According to the Assessment of SpondyloArthritis International Society/European League Against Rheumatism (ASAS/EULAR) 2010 recommendations for AS, all patients should have an adequate trial of at least two nonsteroidal anti-inflammatory drugs (NSAIDs) for pain and stiffness, unless contraindicated. Recommendations for other therapies before receiving Humira (or other TNF blocker therapy) vary according to the manifestations of the disease, level of current symptoms, clinical findings, etc. According to these recommendations, patients with pure axial manifestations do not have to try conventional synthetic DMARDs before anti-TNF agents such as Humira; patients with symptomatic peripheral arthritis should have an
insufficient response to at least one local corticosteroid injection, if appropriate; patients with persistent peripheral arthritis should normally have a trial of a DMARD, preferably sulfasalazine; and patients with enthesitis should try appropriate local therapy (e.g., corticosteroid injection in selected cases). In the AS guidelines, it is recommended to assess a patient’s response to a TNF blocker after at least 12 weeks of therapy.

**Dosing in AS.** Dosage and administration consistent with U.S. Food and Drug Administration approved label (i.e., 40 mg every other week).

3. **Crohn’s Disease in a Patient ≥ 6 Years of Age**

   a) **Initial Therapy.** Approve for 3 months if the patient meets the following criteria (i and ii):
   
   i. Patient meets ONE of the following conditions (1, 2, or 3):
      1. Patient has tried or is currently taking corticosteroids, or corticosteroids are contraindicated in this patient; OR
      2. Patient has tried one other agent for Crohn’s disease (e.g., azathioprine, 6-mercaptopurine, MTX, Cimzia, Remicade, or Entyvio); OR
      3. The patient has had ileocolonic resection (to reduce the chance of Crohn’s disease recurrence); AND
   
   ii. Humira is prescribed by or in consultation with a gastroenterologist.

   b) **Patients Currently Receiving Humira.** Approve for 1 year if the patient has had a response, as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Humira.

   **Note:** Patients with fistulizing Crohn’s disease or Crohn’s disease of the ileal pouch must meet the above criteria for Crohn’s disease in adults.

Humira is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adults with moderately to severely active Crohn’s disease who have had an inadequate response to conventional therapy. Humira is also indicated for reducing signs and symptoms and inducing clinical remission in patients if they have also lost response to or are intolerant to Remicade. In pediatric patients with Crohn’s disease, Humira is indicated for reducing signs and symptoms and inducing and maintaining clinical remission patients 6 years of age and older with moderately to severely active disease who have had an inadequate response to corticosteroids or immunomodulators such as azathioprine, 6-MP, or MTX. There are also published data supporting the use of Humira for prevention of post-operative recurrence of Crohn’s disease. The American Gastroenterological Association (AGA) has guidelines for Crohn’s disease (2013). For induction therapy, TNF blockers are listed as a strong recommendation for patients with moderately severe Crohn’s disease (moderate-quality evidence). TNF blocker ± thiopurine is also mentioned as an appropriate regimen for maintenance of remission.

**Dosing in Crohn’s Disease.** Dosage and administration are consistent with U.S. Food and Drug Administration approved label (i.e., Pediatric 17-<40 kg: 80 mg on day one [given as two 40 mg injections in one day], then 40 mg two weeks later [day 15], followed two weeks later [day 29] with a maintenance dose of 20 mg every or week, ≥ 40 kg: 160 mg on day one
[given as four 40 mg injections in one day or as two 40 mg injections per day for two consecutive days], then 80 mg two weeks later [given as two 40 mg injections in one day] [day 15], followed two weeks later [day 29] with a maintenance dose of 40 mg every other week, Adult: 160 mg on day one [given as four 40 mg injections in one day or as two 40 mg injections per day for two consecutive days], then 80 mg two weeks later [day 15], followed two weeks later [day 29] with a maintenance dose of 40 mg every other week).

4. Juvenile Idiopathic Arthritis (JIA) [or juvenile rheumatoid arthritis (JRA)] (regardless of type of onset)
[Note: This includes patients with juvenile spondyloarthropathy/active sacroiliac arthritis]

a) Initial Therapy. Approve for 3 months if the patient meets the following criteria (i and ii):
   i. The patient meets ONE of the following conditions (1, 2, 3, or 4):
      1. Patient has tried one other agent for this condition (e.g., MTX, sulfasalazine, or leflunomide, a nonsteroidal anti-inflammatory drug [NSAID], or a biologic DMARD [e.g., Enbrel, Ocrecia IV, Remicade, Kineret, Actemra IV]); OR
      2. Patient will be starting on Humira concurrently with MTX, sulfasalazine, or leflunomide; OR
      3. Patient has an absolute contraindication to MTX (e.g., pregnancy, breast feeding, alcoholic liver disease, immunodeficiency syndrome, blood dyscrasias), sulfasalazine, or leflunomide; OR
      4. Patient has aggressive disease, as determined by the prescribing physician; AND

   ii. Humira is prescribed by or in consultation with a rheumatologist.

b) Patients Currently Receiving Humira. Approve for 1 year if the patient has had a response (e.g., has improvement in limitation of motion; less joint pain or tenderness; decreased duration of morning stiffness or fatigue; improved function or activities of daily living; reduced dosage of corticosteroids), as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Humira.

Humira is indicated for reducing signs and symptoms of moderately to severely active polyarticular JIA in patients ages 2 and older. The 2011 ACR recommendations for the treatment of JIA propose initial DMARD treatment with MTX in most patients; however, sulfasalazine is recommended for patients with enthesitis-related arthritis and may also be used in certain patients with sacroiliac arthritis. Leflunomide may be an appropriate initial DMARD in certain patients with high disease activity and/or a poor prognosis. Kineret may be used in systemic arthritis and Actemra may be used in systemic and polyarticular juvenile arthritis arthritis. TNF antagonists such as Humira may also be used as second- or third-line treatment for systemic JIA. The criteria for patients starting on Humira concurrently with a conventional synthetic DMARD or for patients with an absolute contraindication MTX, sulfasalazine, or leflunomide are recommended based on the professional opinion of specialized physicians.
Dosing in Juvenile Idiopathic Arthritis (JIA) [or juvenile rheumatoid arthritis (JRA)]. Dosage and administration consistent with U.S. Food and Drug Administration approved label (i.e., 10-<15 kg: 10 mg every other week, 15-<30 kg: 20 mg every other week; ≥30 kg: 40 mg every other week).

5. Plaque Psoriasis

a) Initial Therapy. Approve for 3 months if the patient meets the following criteria (i and ii):

i. The patient meets ONE of the following conditions (1, 2, or 3):
   1. The patient has tried at least one of the following agents for at least 3 months for plaque psoriasis: an oral therapy for psoriasis (e.g., MTX, cyclosporine, Sotiatane<sup>®</sup> [acitretin tablets]); oral methoxsalen plus ultraviolet A light (PUVA); or a biologic agent (e.g., Enbrel, Remicade, or Stelara); OR
   2. The patient experienced an intolerance to a trial of at least one oral or biologic therapy for plaque psoriasis (e.g., MTX, cyclosporine, Sotiatane, Enbrel, Remicade, or Stelara); OR
   3. The patient has a contraindication to one oral agent for psoriasis such as MTX, as determined by the prescribing physician; AND

ii. Humira is prescribed by or in consultation with a dermatologist.

b) Patients Currently Receiving Humira. Approve for 1 year if the patient has had a response, as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Humira.

Humira is indicated for plaque psoriasis. Guidelines for treatment of plaque psoriasis recommend topical therapy for limited disease. However, for patients with chronic plaque psoriasis that does not respond to topical therapies or patients with more extensive disease, systemic therapy may be used. The traditional systemic agents for plaque psoriasis are MTX, Sotiatane, and cyclosporine. An injectable biologic agent such as Humira is an option for patients who are candidates for phototherapy or systemic therapy, especially those who are intolerant of or unresponsive to traditional systemic agents. In the professional opinion of specialist physicians reviewing the data, we have adopted the criteria requirements for previous therapy.

Dosing in Plaque Psoriasis. Dosage and administration consistent with U.S. Food and Drug Administration approved label (i.e., initial dose of 80 mg, followed by 40 mg given every other week starting one week after the initial dose).

6. Psoriatic Arthritis (PsA)

a) Initial Therapy. Approve for 3 months if Humira is prescribed by or in consultation with a rheumatologist or a dermatologist.

b) Patients Currently Receiving Humira. Approve for 1 year if the patient has had a response (e.g., less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improvements in acute phase reactants [for example, C-reactive protein (CRP)]), as
Humira is indicated for PsA and can be used alone or in combination with DMARDs. In clinical trials, Humira was effective in patients with active PsA despite therapy with an NSAID. There are few well-controlled, prospective studies with adequate duration that have evaluated the efficacy of the oral DMARDs. According to the EULAR recommendations for treatment of PsA (2012), NSAIDs are recommended as first-line treatment. Recommendations for other therapies before receiving a TNF blocker vary according to the manifestations of the disease, prognostic factors, and efficacy/toxicity of previous therapies. The TNF inhibitors indicated in PsA are equally effective for treatment of PsA, inhibition of radiographic progression, and improving physical function in patients with PsA. The conventional synthetic DMARDs have not been shown to prevent the progression of radiographic (structural) damage or to have significant impact on axial disease, dactylitis, or enthesitis in PsA. This is in contrast with the newer biological DMARDs which have shown efficacy in well-controlled trials in reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with PsA.

**Dosing in PsA.** Dosage and administration consistent with U.S. Food and Drug Administration approved label (i.e., 40 mg every other week).

7. **Ulcerative Colitis (UC) in an Adult**

a) **Initial Therapy.** Approve for 3 months if the patient meets the following criteria (i and ii):

   i. The patient meets ONE of the following conditions (1 or 2):

      1. Patient has had a 2-month trial of one systemic agent (e.g., 6-mercaptopurine, azathioprine, cyclosporine, tacrolimus, Remicade, or a corticosteroid such as prednisone or methylprednisolone) or was intolerant to one of these agents for ulcerative colitis; OR

      2. The patient has pouchitis AND has tried therapy with an antibiotic (e.g., metronidazole, ciprofloxacin), probiotic, corticosteroid enema, or Rowasa® (mesalamine) enema; AND

   ii. Humira is prescribed by or in consultation with a gastroenterologist.

b) **Patients Currently Receiving Humira.** Approve for 1 year if the patient has had a response (e.g., decreased stool frequency or rectal bleeding), as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Humira.

Humira is indicated for inducing and sustaining clinical remission of moderately to severely active ulcerative colitis in adults who do not respond to corticosteroids or other immunosuppressive drugs such as azathioprine or 6-mercaptopurine. Clinical guidelines for the management of pouchitis, published in 2009, and ulcerative colitis practice guidelines from the American College of Gastroenterology (ACG) [2010] indicate that first-line therapy for pouchitis is antibiotic therapy (e.g. metronidazole, ciprofloxacin). Other treatment options include maintenance probiotics, oral or topical budesonide, anti-inflammatory drugs (e.g., mesalamine), or immunosuppressive drugs (e.g., Remicade). A retrospective, open-
label, case series demonstrated some efficacy of Humira in patients with pouchitis previously treated with Remicade. In the professional opinion of specialist physicians reviewing the data, we have adopted the criteria requirements for pouchitis.

**Dosing in Ulcerative Colitis.** Dosage and administration consistent with U.S. Food and Drug Administration approved label† (i.e., 160 mg on day one [given as four 40 mg injections in one day or as two 40 mg injections per day for two consecutive days], then 80 mg two weeks later [day 15], followed two weeks later [day 29] with a maintenance dose of 40 mg every other week).

†NOTE: Adalimumab should only be continued when evidence of clinical remission is shown within eight weeks of therapy.

**Other Uses with Supportive Evidence**

8. **Behcet’s Disease**

**Criteria.** Approve for 1 year if the patient meets the following criteria (a and b):

a) The patient meets ONE of the following conditions (i or ii):
   i. The patient has tried at least ONE conventional therapy (e.g., systemic corticosteroids, immunosuppressants [azathioprine, MTX, mycophenolate mofetil, tacrolimus, Leukeran® {chlorambucil}, cyclophosphamide, or cyclosporine], interferon alfa) or Enbrel or Remicade; OR
   ii. The patient has ophthalmic manifestations of Behcet’s disease; AND

b) Humira is prescribed by or in consultation with a rheumatologist, dermatologist, ophthalmologist, gastroenterologist, or neurologist.

Recommendations for the use of TNF blockers in ocular inflammatory disorders from the American Academy of Ophthalmology (AAO) [2014] note that Humira may be used as first-line corticosteroid-sparing therapy in patients with ophthalmmic manifestations of Behcet’s disease. In three cases, Humira was effective in controlling uveitis in adults with Behcet’s disease who were in remission after receiving Remicade. In another case series, six adults with Behcet’s disease (uveitis [two patients], central nervous system disease [two patients], colitis [one patient], and severe oral ulcers and arthritis [one patient]) in whom immunosuppressive therapy had failed, Humira was effective. These patients had received prior therapy with Remicade which had been discontinued after complete response or acceptable improvement. In a retrospective analysis (n = 11), Humira improved visual acuity and showed a corticosteroid and immunosuppressive sparing effect in ocular Behcet’s disease. Another review found 19 patients treated with Humira for Behcet’s disease, all of whom had refractory disease or experienced AEs to cyclosporine and Remicade. Overall, 17 out of 19 patients improved with Humira. In case reports, it has also been effective for neuro-Behcet’s and for treatment of leg ulcers in Behcet’s disease. EULAR recommendations for the management of Behcet disease include either Remicade or cyclosporine in combination with azathioprine and corticosteroids for refractory eye involvement. For gastrointestinal or parenchymal involvement, TNF antagonists have been used in resistant and complicated cases.
9. **Undifferentiated Spondyloarthritis** (Undifferentiated Arthritis)

**Criteria.** Approve for 1 year if Humira is prescribed by or in consultation with a rheumatologist.

Patients may present with signs and/or symptoms of inflammatory arthritis but do not meet diagnostic criteria for any specific type of arthritis. If a clinical work-up does not reveal another diagnosis and clinical presentation does not indicate a specific diagnosis, the patient is often diagnosed with a form of undifferentiated arthritis. Over time, a patient with undifferentiated arthritis may progress to meet the diagnostic criteria for another type of inflammatory arthritis. In a randomized, double-blind trial in patients (n = 185) with nonradiographic axial spondyloarthritis (nr-axSpA), treatment response (ASAS 40) was 36% in patients treated with Humira compared with 15% in patients treated with placebo. However, ASAS 40 response rates were higher in patients with short disease durations, elevated CRP, and active inflammation on magnetic resonance imaging (MRI) of the sacroiliac joints. In a double-blind study in patients (n = 40) with peripheral arthritis who did not meet the criteria for AS or PsA, patient global assessment, physician’s global assessment, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Disease Activity Score (ASDAS), and erythrocyte sedimentation rate (ESR) were significantly improved at Week 12 in the Humira treatment group compared with placebo (P < 0.05 for all comparisons vs. placebo). In a double-blind study conducted at two centers in Germany, 46 patients with active axial spondyloarthritis without radiographically defined sacroiliitis were randomized to placebo or Humira 40 mg EOW for 12 weeks followed by an open-label extension up to Week 52. All patients in the open-label extension received Humira EOW. Patients were refractory to treatment with NSAIDs and had a baseline BASDAI ≥ 4. The Humira dosage was increased to every week in ten patients who did not attain ASAS 40 response after 12 weeks of therapy. At Week 12 an ASAS 40 response (primary endpoint) was attained by 54.5% of the patients on Humira compared with 12.5% with placebo (P = 0.004 vs. placebo). Efficacy was maintained at Week 52. In the entire study group of 46 patients, 50% of patients attained an ASAS 40 response at Week 52. Of note, trials with ankylosing spondylitis include patients who have radiographic changes in the sacroiliac joints which are the consequences of previous inflammation and may take years to become evident.

10. **Uveitis (including other posterior uveitides and panuveitis syndromes)**

**Criteria.** Approve for 1 year if the patient meets the following criteria (a and b):

a) The patient has tried ONE of the following therapies: periocular, intraocular, or systemic corticosteroids; immunosuppressives (e.g., MTX, mycophenolate mofetil, azathioprine, cyclophosphamide, or cyclosporine), Enbrel, or Remicade for this condition; AND

b) Humira is prescribed by or in consultation with an ophthalmologist.

Recommendations for the use of TNF blockers in ocular inflammatory disorders from the AAO (2014) note that Humira may be used in patients with uveitis due to various causes (e.g., spondyloarthropathy-associated or human leukocyte antigen [HLA]-B27-associated uveitis, JIA-associated uveitis, and other posterior uveitides and panuveitis syndromes).
Humira should be considered second-line in vision-threatening JIA-associated uveitis when MTX has failed or is not tolerated (strong recommendation) and may be used as corticosteroid-sparing treatment for vision-threatening chronic uveitis from seronegative spondyloarthritis (strong recommendation). Humira may also be considered in other patients who have vision-threatening or corticosteroid-dependent disease who have failed first-line therapies. The recommendations point out that a prospective study evaluated the efficacy of Humira in patients (n = 31) with a variety of uveitic conditions, including patients with idiopathic panuveitis and patients with birdshot chorioretinitis (BSCR), a bilateral posterior uveitis generally treated with systemic immunomodulation. Results showed a 68% response rate to Humira at Week 10 suggesting efficacy. In patients with uveitis, TNF levels are increased in the serum and aqueous humor. An open-label, uncontrolled study (n = 1,250) showed that treatment with Humira reduced the rate of anterior uveitis flares by 51% in adult patients with anterior uveitis and ankylosing spondylitis (P < 0.001). Other open-label studies and case series have demonstrated efficacy of Humira for treatment in a variety of patients with refractory uveitis. Humira has been effective in a small number of children with chronic uveitis (either with rheumatic disease [JIA] or idiopathic) refractory to other therapies. Humira was also effective in the management of refractory uveitis in adults and has allowed the dose of concomitant immunosuppressives to be reduced.

11. Patient has been Established on Humira for ≥ 90 days
For conditions that do not have criteria for Patients Currently Receiving Humira but are indications or conditions addressed as an approval in the Recommended Authorization Criteria section (FDA-Approved Indications and Other Uses with Supportive Evidence), approve Humira for 1 year, if the patient is currently taking Humira for ≥ 90 days.

Exclusions:
Coverage of Humira is recommended in circumstances that are listed in the Recommended Authorization Criteria (FDA-Approved Indications and Other Uses with Supportive Evidence). The following provides rationale for specific Exclusions. This is not an exhaustive list of Exclusions.

1. Concurrent Use with a Biologic DMARD or Targeted Synthetic DMARD. Humira should not be administered in combination with another biologic agent for an inflammatory condition (e.g., TNF antagonists [Cimzia, Enbrel, Remicade, Simponi SC, or Simponi Aria], Actemra, Kineret, Orencia, or Rituxan® [rituximab for IV infusion], or Stelara). Combination therapy with two biologic agents is not recommended due to a higher rate of AEs with combinations and/or lack of additive efficacy. Xeljanz should not be used in combination with biologic DMARDs such as Humira. Targeted synthetic DMARDs (e.g., Xeljanz, Otezla) do not have data supporting use in combination with biologic DMARDs. Do to similar safety concerns (i.e., increased risk of AEs) plus no evidence of additive efficacy, targeted synthetic DMARDs should not be used in combination with biologic DMARDs such as Humira. Note: This does NOT exclude the use of conventional synthetic DMARDs (e.g., MTX, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with Humira.

2. Osteoarthritis. In an open-label trial in 12 patients with moderate to severe erosive/inflammatory osteoarthritis of the hands despite therapy with NSAIDs, 12 weeks of therapy with Humira 40 mg EOW did not significantly improve signs and symptoms
(number of tender joints, grip strength, disability, pain, or global disease assessment). Another study randomized patients with radiographic erosive OA of the interphalangeal joints (n = 60) to treatment with Humira 40 mg or placebo EOW for 52 weeks. OA progressed to erosive disease more often in joints with soft-tissue swelling at baseline (14.5% of joints with baseline inflammation treated with placebo [9/62 joints] vs. 3.7% treated with Humira [3/81 joints]; P = 0.009). At Week 52, active disease was similar in both groups, and there was not a statistically significant difference in clinical outcomes, including pain, stiffness, function, number of tender joints or joints with palpable effusion, or maximal grip strength. Larger, long-term, placebo-controlled trials that have a specific efficacy outcome for hand or generalized osteoarthritis are needed.

3. **Hidradenitis Suppurativa.** A 16-week, Phase II, parallel, randomized, placebo-controlled study with an open-label 36-week period evaluated Humira in adult patients with moderate to severe hidradenitis suppurativa (n = 154). Patients were randomized in a 1:1:1 ratio to treatment with Humira 40 mg/week, Humira 40 mg every other week (EOW), or placebo. Following the 16-week randomized portion of the study, all patients received Humira 40 mg EOW but were allowed to switch to weekly dosing if a suboptimal response was achieved at Week 28 or Week 31. At Week 16, 3.9%, 9.6%, and 17.6% of patients in the placebo, Humira EOW, and Humira weekly groups, respectively, achieved a clinical response, measured by the proportion of patients achieving a hidradenitis suppurativa Physician’s Global Assessment (PGA) score of clear, minimal, or mild with at least a 2-grade improvement relative to baseline (statistically significant for Humira weekly compared to placebo [P = 0.025]). Mean reductions in the Dermatology Life Quality Index (DLQI) between baseline and Week 16 were 2.3, 3.2, and 6.3 for patients in the placebo, Humira EOW, and Humira weekly treatment groups, respectively (statistically significant for Humira weekly vs. placebo [P = 0.001]). Other significant improvements were noted in patient-reported outcomes and pain in the Humira weekly group compared to the placebo group. During the open-label phase, the proportion of patients with a clinical response decreased after the change from weekly dosing to EOW dosing (i.e., 63% had a suboptimal response and were escalated to weekly dosing). Of the 89 patients whose dose was escalated, 15% of patients (n = 13) had a clinical response at Week 52. Other small studies and case reports have also demonstrated efficacy of Humira for treatment of hidradenitis suppurativa.

4. **Pyoderma Gangrenosum.** Multiple topical and systemic therapies have been used to treat pyoderma gangrenosum. Oral prednisone is the most common initial immunosuppressant medication. Topical therapies (e.g., corticosteroids, immunomodulators) may be applied to the lesion. Other systemic therapies used for treatment of pyoderma gangrenosum include cyclosporine, MTX, azathioprine, cyclophosphamide, mycophenolate mofetil, Remicade, Enbrel, and Humira. In case reports, Humira and other TNF antagonists have been effective in treating pyoderma gangrenosum.

5. **Sarcoidosis.** Well-controlled studies are not available for any therapies. Steroids are the standard therapy, though long-term use is limited by AEs. Immunosuppressants have shown modest efficacy with the best results available for MTX. High levels of TNF in bronchoalveolar lavage of patients with sarcoidosis have been reported with a decrease in TNF levels following treatment. Recommendations for best practice in the management of pulmonary and systemic sarcoidosis recommend glucocorticoids as first-line therapy. Patients who cannot be weaned to a prednisone-equivalent dose of < 10 mg/day are
appropriate candidates for steroid-sparing treatment with cytotoxic agents (e.g., MTX, azathioprine, leflunomide). If these agents fail or cause toxicity, Humira, Remicade, cyclophosphamide, or mycophenolate mofetil are proposed. In a double-blind, placebo-controlled study, Humira was effective in improving clinical lesions and DLQI score in patients with cutaneous sarcoidosis (n = 16). In a prospective study in patients with refractory posterior uveitis (n = 26), intraocular inflammation improved and other indicators of disease activity, including pulmonary lung tests and laboratory tests, improved with Humira. Humira has also been effective in case reports of patients who were refractory to standard therapy. Recommendations for the use of TNF blockers in ocular inflammatory disorders from the AAO (2014) note that Remicade or Humira may be considered as second-line immunomodulatory therapy for patients failing or intolerant of standard immunomodulatory agents (e.g., prednisone and MTX).

6. **Scleritis or Sterile Corneal Ulceration.** Recommendations for the use of TNF blockers in ocular inflammatory disorders from the AAO (2014) mention Humira as an agent that should be considered as a second-line immunomodulatory agent for severe ocular inflammatory conditions including chronic and severe scleritis.

7. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.