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Medication Policy Manual

Policy No: dru081

Topic: Humira[®], adalimumab

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IMPORTANT REMINDER

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Adalimumab (Humira[®]) binds to and inhibits the activity of tumor necrosis factor (TNF), a chemical that causes inflammation. Adalimumab is used for the treatment of rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, juvenile idiopathic arthritis, Crohn's disease and plaque psoriasis.

Policy/Criteria

- I.** Most contracts require prior authorization approval of adalimumab prior to coverage. Adalimumab may be considered medically necessary for treatment of the conditions listed below when at least one of criteria A through E below is met.

- A. Psoriatic arthritis** when the diagnosis is established by a rheumatologist or a dermatologist.

OR

- B. Ankylosing spondylitis** when the diagnosis is established by a rheumatologist.

OR

- C. Rheumatoid arthritis (RA) or juvenile idiopathic arthritis (JIA) when:**

1. There is a diagnosis that has been established by a rheumatologist (or, for RA, by the criteria in Appendix 1).

AND

2. Methotrexate is ineffective after at least a 6 to 12 week treatment course based on documentation which includes one or more of the assessment components listed in Appendix 2 except if methotrexate is contraindicated or not tolerated based on clinical documentation.

OR

- D. Crohn's disease** – Initial authorization for adalimumab may be considered medically necessary for:

1. Fistulizing Crohn's disease.

OR

2. Acute treatment of an exacerbation of Crohn's disease when at least one of the following criteria a, b or c below is met:

- a.** Treatment with an adequate course of systemic corticosteroids (e.g., 40 mg to 60 mg prednisone per day for 7 to 14 days) has been ineffective or is contraindicated.

OR

- b.** The patient has been unable to taper off of an adequate course of systemic corticosteroids without experiencing worsening of disease.

OR

- c. The patient is experiencing breakthrough disease (e.g., active disease flares) while stabilized for at least 2 months on an immunomodulatory medication (such as azathioprine, mercaptopurine, cyclosporine, or methotrexate).

OR

3. Acute and/or maintenance treatment of Crohn's Disease when infliximab (Remicade) has been ineffective or not tolerated.

OR

E. Chronic plaque psoriasis: Initial authorization for adalimumab may be considered medically necessary for patients when all of the following criteria (1 through 4 below) are met:

1. Chart notes support a diagnosis of chronic plaque psoriasis involving at least 10% of the body surface area or causes significant functional disability.

AND

2. The prescribing physician is a dermatologist or rheumatologist.

AND

3. Treatment with phototherapy or photochemotherapy was ineffective, contraindicated, or not tolerated (see Appendix 3).

AND

4. Treatment with at least one systemic agent for psoriasis was ineffective or not tolerated, unless all are contraindicated. Examples of systemic agents include, but are not limited to, cyclosporine, methotrexate, and acitretin.

II. Administration, Quantity Limitations, and Authorization Period

- A.** Regence considers adalimumab to be a self-administered medication.
- B.** When prior authorization is approved, adalimumab may be authorized in quantities as follows:
 1. **Rheumatologic conditions** (Rheumatoid arthritis, Psoriatic arthritis, Ankylosing spondylitis, Juvenile idiopathic arthritis): 40 mg every 2 weeks.

2. Crohn's disease

a. **Initial Authorization:** When prior authorization is approved, adalimumab may be covered in quantities up to 12 of the 40 mg vials in the initial 3 month period (induction period).

b. **Continued Authorization:** If documentation is provided that the initial 3 month treatment period was effective, adalimumab may be covered in quantities of 40 mg every 2 weeks.

3. **Chronic plaque psoriasis:** When prior authorization is approved, adalimumab may be covered in quantities of 4 of the 40 mg vials (160 mg) in the first month, then in quantities of 40 mg every 2 weeks thereafter.

C. **Authorization Period:** Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

III. Adalimumab is considered not medically necessary when used in maintenance doses exceeding 40 mg every 2 weeks.

IV. Adalimumab is considered investigational when used for all other conditions, including, but not limited to:

A. Use in combination with a tumor necrosis factor (TNF) or interleukin-1 (IL-1) inhibitor, such as infliximab, etanercept or anakinra.

B. Blau's Syndrome (familial juvenile systemic granulomatosis).

C. Erosive/inflammatory osteoarthritis.

D. Pulmonary sarcoidosis.

E. Reactive arthritis.

F. Ulcerative colitis.

Position Statement

Treatment of rheumatic disorders (rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, ankylosing spondylitis) ^[1,34-41, 45, 47]

- There are many treatments for rheumatic disorders that are effective, have known long-term safety profiles, and are recommended by national treatment guidelines.

- Non-medical therapies, such as prescribed exercise therapy, physical therapy and weight loss, are important components in any treatment plan for patients suffering from a rheumatic disorder.
- When a systemic medication therapy is needed to manage one of the rheumatic disorders, oral therapies are usually the best value.
 - * Medications to control inflammation, such as non-steroidal anti-inflammatory medications (e.g., meloxicam, nabumetone, and naproxen) and glucocorticoids (oral and injected into the joint) are effective for the management of symptoms, particularly during the early stages of disease.
 - * Orally administered disease-modifying antirheumatic drugs (DMARDs), including methotrexate (MTX), hydroxychloroquine, leflunomide, and sulfasalazine, are effective for decreasing symptoms and slowing disease progression, have a proven track record, and have been the standard of care for many years.
 - * Oral therapies have known potential risks. The management of these risks is well established.
- Methotrexate is considered effective in the treatment of RA and the standard reference DMARD to which newer DMARDs (etanercept, anakinra, adalimumab, and leflunomide) are compared for efficacy.
- When non-medical therapies and oral medications are inadequate, the biologic medications (e.g., adalimumab, etanercept, infliximab, or abatacept) may be appropriate. Certolizumab and rituximab have been studied in RA, but their role in therapy remains uncertain at this time.
- No studies have shown that any one biologic medication is more effective than another in the treatment of rheumatic disorders, with the exception of indirect evidence that anakinra may be less effective than other alternatives.
 - * The biologic agents can decrease symptoms, help preserve joint functioning, and slow the progression of rheumatic disease.
 - * There are no reliable, direct comparative trials that have demonstrated a difference in clinical effect or safety of one agent over another.
 - * Individual responses and tolerability are unpredictable and may vary between patients.
 - * Because responses vary, if one of the biologic agents provides an inadequate response, another biologic medication may yet be effective.

- * In RA, the best response is seen when methotrexate is used concomitantly with any of the biologics. Infliximab has been shown to be effective only when used with methotrexate.

Efficacy of biologic agents in rheumatic conditions ^[1,34-41, 45, 47]

The benefit of medications can be indirectly compared by calculating their number needed to treat (NNT). The number needed to treat is a measure of the chances of a patient achieving a benefit (how many patients need to be treated before a benefit is achieved over a certain period of time). The lower the number needed to treat, the more likely the medication will have benefit.

Table 1 summarizes the chances that certain biologic rheumatologic medications will improve joint pain and stiffness in rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis:

Table 1: Chances of improving joint pain and stiffness by at least 20% after six months of treatment with biologic medications (compared to no treatment). ^[1,34-41, 45, 47]			
Biologic Medications (when used with methotrexate)	Rheumatoid Arthritis	Psoriatic Arthritis	Ankylosing Spondylitis
adalimumab (Humira) etanercept (Enbrel) infliximab (Remicade)	About 1 in 3 likely to benefit ^a NNT = 3 (Range 2-4)	About 1 in 3 likely to benefit ^a NNT = 3	About 1 in 4 likely to benefit ^a NNT = 4 (Range 3-4)
abatacept (Orencia)	About 1 in 4 likely to benefit ^a NNT = 4 (Range 3-4)	N/A	N/A
anakinra (Kineret)	About 1 in 7 likely to benefit ^a NNT = 7	N/A	N/A
certolizumab (Cimzia)	Uncertain ^b	N/A	N/A
rituximab (Rituxan)	Uncertain ^b	N/A	N/A

^a Benefit = at least 20% improvement in joint pain and stiffness after six months of treatment.

^b The trials for these medications had flaws that make estimating their efficacy uncertain. These flaws included large numbers of patients not completing the clinical trials, not all patients counted in the final results, and uncertainty about whether patients and caregivers were truly unaware of the assigned treatments.

- There is reliable evidence that etanercept, adalimumab, and abatacept (when given with methotrexate) are effective in the management of patients with juvenile idiopathic arthritis (JIA). The design of the clinical studies prevents calculation of “number-needed-to-treat” (NNT) for this use. ^[1, 34, 37]

Efficacy of adalimumab in rheumatoid arthritis (RA)

- Reliable clinical trials show compelling evidence that adalimumab (in combination with methotrexate) achieves significant clinical and radiographic improvements in RA patients who have an inadequate response to methotrexate. ^[1,17,33,34]
- The recommended dose for adalimumab for adult patients with RA is 40 mg administered every 2 weeks as a subcutaneous injection. ^[1]
- If adalimumab 40 mg every other week as monotherapy does not result in an adequate response, methotrexate or another oral DMARD may be added to increase the effectiveness of treatment.
- Methotrexate in combination with adalimumab (40 mg every 2 weeks) appears to result in larger proportions of patients achieving ACR 20, 50, and 70 responses than adalimumab monotherapy (40 mg every 2 weeks OR 40 mg weekly). ^[1,16] This observation has been replicated in other published reports and for other DMARDs. ^[30,31]
- Patients who have an inadequate response to other TNF- α inhibitors may still receive benefit from switching to adalimumab. ^[32,33]

Efficacy of adalimumab in psoriatic arthritis (PSA)

- Adalimumab improves joint-related and skin-related symptoms in patients with moderate-to-severe psoriatic arthritis. ^[1,12,27-29]
- In a reliable, double-blind, randomized, placebo-controlled trial, treatment with adalimumab (40 mg every other week) resulted in improvements in disease activity as compared to treatment with placebo in patients with psoriatic arthritis. ^[1,12] Statistically significant differences were seen in ACR20 scores at week 12 and in the modified total Sharp score of structural damage at week 24 (both primary endpoints).
 - * Patients who completed 24 weeks of treatment were allowed to continue treatment with adalimumab in an open-label fashion for up to 48 weeks. At week 48, 56% of patients continuing achieved ACR 20 improvement in their arthritis symptoms, and 58% of patients achieved PASI 75 improvement in their psoriasis symptoms. ^[27]
- The recommended dose of adalimumab for adult patients with psoriatic arthritis is 40 mg administered every other week as a subcutaneous injection. ^[1] Other DMARDs may be continued during treatment with adalimumab.

- There are no data available to support any additional benefit of increasing the dose of adalimumab to 40 mg every week in patients with psoriatic arthritis.

Efficacy of adalimumab in ankylosing spondylitis (AS)

- Adalimumab has demonstrated clinical benefit in patients active ankylosing spondylitis. [1,15,23,24]
 - * In a reliable multicenter, randomized, double-blind, placebo controlled trial, treatment with adalimumab (40 mg every other week) resulted in improvements in disease activity as compared to placebo in patients treated for 12 weeks.
 - * More patients who received adalimumab (58%) achieved a 20% improvement in disease symptoms (ASAS20) at week 12 compared to patients who received placebo (21%). (ASAS20 is a 20% improvement in disease symptoms as measured by the Assessment in Ankylosing Spondylitis International Working Group criteria for improvement, and is considered a meaningful response to therapy.
- There are no data available to support additional benefit with doses of adalimumab greater than 40 mg every other week. [1]

Efficacy of adalimumab in polyarticular juvenile idiopathic arthritis (juvenile rheumatoid arthritis) (JIA)

- The safety and efficacy of adalimumab were assessed in a multicenter, randomized, withdrawal, double-blind, parallel-group study in 171 children (4 to 17 years of age) with polyarticular juvenile idiopathic arthritis (JIA). [1]
- - * All included subjects had to show signs of active moderate or severe disease despite previous treatment with NSAIDs, analgesics, corticosteroids, or DMARDs.
 - * The combination of adalimumab and methotrexate appears to be more effective than adalimumab alone. Ninety-four percent of children who received adalimumab 24 mg/m² (max 40 mg) with methotrexate (MTX) achieved a 30% improvement in Pediatric ACR30 response compared to 74% of children who received adalimumab alone.
 - * Among children who initially respond to adalimumab, continuation decreases the chance of future disease flares compared to children who stopped adalimumab.

Treatment of Crohn's disease and ulcerative colitis [1,34-40, 42, 43]

- There are many treatments for Crohn's disease (CD) and ulcerative colitis (UC) that are effective, have known long-term safety profiles, and are recommended by national treatment guidelines.

- Lifestyle interventions, such as smoking cessation and diet modification, are important components of a comprehensive treatment plan for patients suffering from CD.
- When medication therapy is needed to manage CD and UC, oral and topical (administered rectally) therapies are often the best value.
 - * First-line therapies to induce remission include:
 - For patients with CD: oral corticosteroids, methotrexate, aminosalicylates, azathioprine, mercaptopurine.
 - For patients with UC: oral aminosalicylates (e.g., sulfasalazine), topical mesalamine (i.e., rectally administered), topical corticosteroids, or oral corticosteroids, depending on the extent and location of disease.
 - Due to the potential for severe adverse effects, the use of conventional corticosteroids such as prednisone is generally reserved for patients with moderate to severe disease who failed to respond to first-line therapies. Use is generally limited in duration and frequency.
 - Corticosteroids such as prednisone are effective in both patients with Crohn's disease and patients with ulcerative colitis. Dosages in the range of 40 mg – 60 mg/day or 1 mg/kg/day of prednisone or equivalent are effective for induction of remission.^[49-51]
 - * First-line therapies to maintain remission include:
 - For patients with CD: methotrexate and azathioprine.
 - For patients with UC: topical mesalamine (i.e., rectally administered), oral aminosalicylates (e.g., sulfasalazine), topical corticosteroids, or oral corticosteroids, depending on the extent and location of disease.
- When non-medical therapies and oral/topical medications are inadequate, the biologic medications, adalimumab (CD only) or infliximab (CD and UC) may be appropriate. Certolizumab and natalizumab have been studied in CD, but their roles in therapy remain uncertain at this time.
- There is inadequate evidence to show that one TNF- α inhibitor is more effective than another for the management of patients with moderate-to-severe Crohn's disease.
 - * Generally, these medications result in a remission of disease in about 1 in every 5 to 8 patients when compared with a placebo agent.
 - * There have been no direct-comparative trials that have demonstrated a difference in clinical effect or safety of one agent over another.

- * There is inadequate evidence to establish the efficacy of certolizumab in fistulizing Crohn's disease.
- Because of the risk of serious (sometimes fatal) adverse events with natalizumab, it is recommended that it only be used after other treatment options have failed.
- In this class of medications, only infliximab has been adequately studied in the management of patients with ulcerative colitis.

Efficacy biologic agents in Crohn's disease and ulcerative colitis ^[1,34-40, 42, 43]

The benefit of medications can be indirectly compared by calculating their number needed to treat (NNT). The number needed to treat is a measure of the chances of a patient achieving a benefit (how many patients need to be treated before a benefit is achieved over a certain period of time). The lower the number needed to treat, the more likely the medication will have benefit.

Table 2 summarizes the chances that certain biologic medications will improve disease symptoms such as the number and consistency of stools, pain, associated conditions, or weight loss, either initially or as on-going treatment, in patients with Crohn's disease or ulcerative colitis. ^{a,b}

Table 2: Chances of significantly improving symptoms of Crohn’s disease or ulcerative colitis with biologic medications (compared to no treatment). ^[1,34-40, 42, 43]			
Biologic Medications	Crohn’s Disease		Ulcerative Colitis
	Initial Treatment	Ongoing Treatment (6 months of treatment)	Ongoing Treatment (6 months of treatment)
infliximab (Remicade)	About 1 in 3 likely to benefit after 10 weeks of initial treatment NNT = 3	About 1 in 7 patients likely to benefit. NNT = 7 (range 5 - 8)	About 1 in 4 patients likely to benefit. NNT = 4 (range 3 – 5)
adalimumab (Humira)	About 1 in 7 patients likely to benefit after 6 weeks of treatment. NNT = 7 (range 5 – 8)	About 1 in 5 patients likely to benefit. NNT = 5	N/A
certolizumab (Cimzia)	Uncertain ^c		Not studied
natalizumab (Tysabri)	Uncertain ^c		Not studied

^a Crohn’s Disease: Benefit means control of symptoms, otherwise known as “remission”, defined as a total symptom score of no more than 150 on the Crohn’s Disease Activity Index (CDAI), a standard grading system for Crohn’s disease symptoms. This represents a significant improvement in Crohn’s disease symptoms.

^b Ulcerative colitis: Benefit means control of symptoms, otherwise known as “clinical response”, defined as a decrease from baseline in the Mayo score by 30% or more and 3 points or more, accompanied by a decrease in the rectal bleeding sub-score of 1 or more or a rectal bleeding sub-score of 0 or 1. These are standard measures of the severity of symptoms in ulcerative colitis, and represent a significant improvement in ulcerative colitis disease symptoms.

^c The trials for these medications had flaws that make estimating their efficacy uncertain. These flaws included large numbers of patients not completing the clinical trials, not all patients counted in the final results, and uncertainty about whether patients and caregivers were truly unaware of the assigned treatments.

Efficacy of adalimumab in achieving remission in Crohn's disease

- In a short, reliable, double-blind, dose ranging trial (CLASSIC-I), a two-dose induction regimen was shown to result in disease remission in patients receiving adalimumab 80 mg/40 mg (24%, $p=0.06$ vs. placebo), adalimumab 160 mg/80 mg (36%, $p=0.001$ vs. placebo), or placebo (12%) at weeks 0 and 2 4 weeks after treatment initiation. ^[18]
- In a continuation of the CLASSIC-I trial, the CLASSIC-II trial evaluated 56 patients who had achieved remission after the two-dose induction regimen. Patients were randomized to receive adalimumab 40 mg every other week (every other week, $n=19$), adalimumab 40 mg weekly ($n=18$) or placebo ($n=18$). ^[19]
 - * At the end of 56 weeks, 79% of patients receiving adalimumab 40 mg every other week and 83% of patients receiving adalimumab 40 mg weekly achieved remission (CDAI score < 150 points) vs. 44% of patients receiving placebo ($p<0.05$ for each adalimumab group vs. placebo).
 - * There was no statistical difference in the number of patients achieving remission between the adalimumab every other week and weekly groups.

Efficacy of adalimumab in maintaining remission in Crohn's disease.

- In a 56-week, randomized, placebo-controlled trial of adalimumab to induce and maintain remission in patients with moderately to severely active Crohn's disease (CHARM) showed that an induction dose of 80 mg on week 0 and 40 mg on week two, followed by either 40 mg administered subcutaneously every week or every other week, both induced and maintained a greater clinical response compared to placebo. ^[20]
 - * Of the 854 patients enrolled in the trial, 499 (58%) had a responded to the induction and were randomized. At week 56, 36% of patients receiving adalimumab 40 mg every other week and 41% of patients receiving adalimumab 40 mg weekly achieved remission (CDAI score < 150) vs. 12% of patients receiving placebo ($P<0.001$ vs. placebo).
 - * At week 56, complete fistula closure was achieved by 33% of patients receiving adalimumab (both doses combined) vs. 13% of patients receiving placebo ($p=0.016$).
 - * Doses of adalimumab higher than 40 mg every other week did not result in increased therapeutic benefit. ^[19,20]
- In a randomized, placebo-controlled induction study, 325 patients with Crohn's disease who had lost response to treatment with, or were intolerant to, previous infliximab therapy, were randomized to receive adalimumab 160 mg and 80 mg on weeks 0 and 2, or placebo. At week 4, 21% of patients treated with adalimumab had achieved remission compared with 7% of patients receiving placebo ($P<0.001$, ABI 14%, NNT=8). ^[26]
- There are no trials comparing adalimumab to any other treatment for Crohn's disease.

Treatment of plaque psoriasis [1,34-40, 44]

- There are many treatments for psoriasis that are effective, have known long-term safety profiles, and are recommended by national treatment guidelines.
 - * Light therapy, including UVB and PUVA is very effective and safe. UVB therapy can be used at home, as well at the doctor's office. PUVA has the potential to cause long term remissions.
 - * When systemic therapy is needed to manage psoriasis, oral therapies are the best value.
 - Oral therapies, including methotrexate and cyclosporine, have a proven track record and have been the standard of care for many years.
 - Oral medications are effective for most patients, and cyclosporine is known to work rapidly.
 - Oral therapies have known potential risks. The management of these risks is well established.
- When oral medications and phototherapy is inadequate, the biologic medications (e.g., adalimumab, etanercept, infliximab, efalizumab, alefacept) may be appropriate. Each of these biologics been shown to be effective for psoriasis.
- There are no studies showing that any one TNF- α inhibitor (etanercept, adalimumab, and infliximab) is more effective than another.
- Alefacept and efalizumab are also effective in some patients, but there is indirect evidence that they may be less effective than other alternatives.
- Individual responses and tolerability are unpredictable and may vary between patients.
- Because responses vary, if one of the biologic agents provides an inadequate response, another biologic medication may yet be effective.

Efficacy of biologic agents in plaque psoriasis [1,34-40, 44]

The benefit of medications can be indirectly compared by calculating their number needed to treat (NNT). The number needed to treat is a measure of the chances of a patient achieving a benefit (how many patients need to be treated before a benefit is achieved over a certain period of time). The lower the number needed to treat, the more likely the medication will have benefit.

Table 3 summarizes the chances that certain biologic medications will improve size and thickness of skin lesions, redness, and itching in moderate to severe plaque psoriasis:

Table 3: Chances of improving of skin lesions, redness, and itching, by 75% after 12 to 16 weeks of treatment with biologic medications (compared to no treatment). ^[1,34-40, 44]

Medications	Benefit In Moderate To Severe Plaque Psoriasis
etanercept (Enbrel), adalimumab (Humira), infliximab (Remicade)	About 1 in 3 likely to benefit ^a NNT = 3 (Range 2-4)
alefacept (Amevive)	About 1 in 9 likely to benefit ^a NNT = 9 (Range 2 – 4)
efalizumab (Raptiva)	About 1 in 5 likely to benefit ^a NNT = 5 (Range 3 – 6)

^a Benefit = at least 75% improvement in size and thickness of skin lesions, redness, and itching after 12 to 16 weeks of treatment.

Efficacy of adalimumab in plaque psoriasis

- Adalimumab was shown to be safe and effective for the treatment of psoriasis in two reliable, phase III, randomized, controlled trials.
- In a randomized, double-blind, placebo controlled trial, 1,212 patients with moderate-to-severe plaque psoriasis were randomized (2:1) to receive adalimumab 80 mg on week 0 then 40 mg every other week x 16 weeks or placebo. Responders continued on for up to 36 additional weeks, then were re-randomized to receive adalimumab or placebo up to week 52. At 16 weeks, 71% of patients receiving adalimumab achieved a PASI 75 score as compared to 7% of patients receiving placebo. (P<0.001, NNT = 2) ^[21]
- In another randomized, double-blind, double-dummy, placebo-controlled study, 271 patients with moderate-to-severe plaque psoriasis were randomized to receive adalimumab 80 mg on week 0 then 40 mg every other week x 16 weeks, methotrexate 7.5 mg PO weekly, titrated up to 25 mg weekly by week 12, for a total duration of 16 weeks, or placebo. ^[22]
 - * At week 16, 80% of patients receiving adalimumab and 36% of patients receiving methotrexate achieved PASI 75 scores, compared with 19% of patients receiving placebo. (P<0.001 for both treatments vs. placebo). NNT for adalimumab and methotrexate vs. placebo were, respectively 2 and 6.
 - * When adalimumab was compared to methotrexate, the NNT was 3.

Use of adalimumab in other conditions

BLAU’S SYNDROME (FAMILIAL JUVENILE SYSTEMIC GRANULOMATOSIS)

- No randomized, controlled trials have been published evaluating the use of adalimumab in patients with Blau’s syndrome.

EROSIVE/INFLAMMATORY OSTEOARTHRITIS

- A small, open-label pilot trial of adalimumab in 12 patients with erosive/inflammatory osteoarthritis did not demonstrate a significant benefit as measured by ACR20 after 4 weeks of treatment. ^[25]

PULMONARY SARCOIDOSIS

- No randomized controlled trials have been published evaluating the use of adalimumab in patients with pulmonary sarcoidosis.

REACTIVE ARTHRITIS

- No randomized controlled trials have been published evaluating the use of adalimumab in patients with reactive arthritis.

ULCERATIVE COLITIS

- No randomized controlled trials have been published evaluating the use of adalimumab in patients with ulcerative colitis.

Safety of adalimumab

- The prescribing information includes warnings that: ^[1]
 - * Tuberculosis (TB), invasive fungal, and other opportunistic infections (some fatal) have occurred in patients treated with adalimumab.
 - * Serious infections and sepsis, including fatalities, have been reported with the use of TNF-blocking agents including adalimumab.
 - * Physicians should exercise caution when considering the use of adalimumab in patients with a history of recurrent infection or underlying conditions which may predispose them to infection or patients who have resided in regions where tuberculosis and histoplasmosis are endemic.
 - * Prescribers should exercise caution in considering the use of adalimumab in patients with pre-existing or recent-onset central nervous system demyelinating disorders.
- In the controlled portions of clinical trials of some TNF-blockers agents, including adalimumab, more cases of malignancies and lymphomas have been observed among patients receiving those TNF-blockers compared to patients in the control group.
- The evidence on TNF-blockers such as Humira suggests that the risk of malignancies in patients with rheumatoid arthritis treated with these medications increases with the use of higher doses. ^[46]

Appendix 1: American College of Rheumatology (ACR) Classification Criteria for Establishing the Diagnosis of Rheumatoid Arthritis (RA) ^[13]

Diagnosis of RA requires the presence of at least 4 of 7 criteria below:

- | | |
|----|--|
| 1. | Morning stiffness in and around joints lasting more than 1 hour. |
| 2. | Arthritis in at least 1 area in a wrist or proximal interphalangeal (PIP) joint (hands or fingers) for > 6 weeks. |
| 3. | Simultaneous swelling or fluid accumulation in 3 or more joints for > 6 weeks. |
| 4. | Symmetric (bilateral joint) involvement for > 6 weeks. |
| 5. | Presence of rheumatoid nodules. |
| 6. | Positive serum rheumatoid factor. |
| 7. | Radiographic changes typical of RA (erosion or unequivocal bony decalcification in or adjacent to the involved joint) on hand and wrist are present. |

Appendix 2: American College of Rheumatology (ACR) Assessment Components for Improvement in Rheumatoid Arthritis (RA) ^[14]

- | | |
|---|--|
| - | Tender joint count. |
| - | Swollen joint count. |
| - | Patient's assessment of pain. |
| - | Patient's global assessment of disease activity. |
| - | Physician's global assessment of disease activity. |
| - | Patient's assessment of physical function. |
| - | Acute phase-reactant measures (erythrocyte sedimentation rate or C-reactive protein levels). |

Appendix 3: Absolute and Relative Contraindications for Phototherapy or Photochemotherapy

Situations where phototherapy may be absolutely or relatively contraindicated include:

- Type 1 or type 2 skin
- History of photosensitivity
- Treatment of facial lesions
- Presence of premalignant lesions
- History of melanoma or squamous-cell carcinoma
- Physical inability to stand for the required exposure time

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Cross References
Enbrel [®] , etanercept dru035
Kineret [®] , anakinra dru049
Remicade [®] , infliximab dru036
Amevive [®] , alefacept dru088
Raptiva [®] , efalizumab dru104
Orencia [®] , abatacept dru129
Cimzia [®] , certolizumab dru160

Codes	Number	Description
		Retail Prescription Drug
HCPCS	J0135	Humira 20 mg/0.4ml kit, Humira 40 mg/0.8 mL kit, Humira Pen 40 mg/0.8 mL kit, Humira Pen Starter 40 mg/0.8 mL kit
	NOTE:	Humira is a self-administered injectable medication and is covered according to the member's benefit for self-administered injectables.