HUMIRA® (ADALIMUMAB)

UTILIZATION MANAGEMENT CRITERIA

<table>
<thead>
<tr>
<th>DRUG CLASS:</th>
<th>Biologic Disease Modifying Anti-Rheumatic Drug (DMARD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAND (generic) NAMES:</td>
<td>Humira (adalimumab injection)</td>
</tr>
<tr>
<td>• Injection: 40 mg/0.8 mL in a single-use prefilled pen (Humira Pen)</td>
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<tr>
<td>• Injection: 40 mg/0.8 mL in a single-use prefilled glass syringe</td>
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<tr>
<td>• Injection: 20 mg/0.4 mL in a single-use prefilled glass syringe</td>
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<tr>
<td>• Injection: 40 mg/0.8 mL in a single-use glass vial</td>
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FDA-APPROVED INDICATIONS

Adalimumab is a tumor necrosis factor (TNF) blocker indicated for the treatment of:

- **Rheumatoid arthritis**: Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis.
- **Polyarticular juvenile idiopathic arthritis (JIA) in patients aged 4 years or older**: Reducing signs and symptoms of moderately to severely active polyarticular JIA in pediatric patients 4 years of age and older.
- **Psoriatic arthritis**: Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active psoriatic arthritis.
- **Ankylosing Spondylitis**: Reducing signs and symptoms in adult patients with active ankylosing spondylitis.
- **Plaque Psoriasis**: Treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate.
- **Crohn’s Disease**: Reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn’s disease who have had an inadequate response to conventional therapy. Adalimumab is indicated for reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab.
- **Ulcerative Colitis**: Inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine (6-MP). The effectiveness of adalimumab has not been established in patients who have lost response to or are intolerant to TNF blockers.
- **Hidradenitis Suppurativa**: Treatment of adult patients with moderate to severe hidradenitis suppurativa.
COVERAGE AUTHORIZATION CRITERIA

Coverage is provided for **Ankylosing Spondylitis** if:
1. Patient is an adult (≥ 18 years of age) with active ankylosing spondylitis.

Coverage is provided for **Hidradenitis Suppurativa** if:
1. Patient is an adult (≥ 18 years of age) with moderate to severe hidradenitis suppurativa.

Coverage is provided for **Crohn’s Disease** if:
1. Patient is an adult (≥ 18 years of age) with moderately to severely active Crohn’s disease, **AND**
2. The patient has experienced a therapeutic failure or inadequate response to conventional therapy (e.g., corticosteroids, 5-aminosalicylate, azathioprine, 6-mercaptopurine, metronidazole, methotrexate); **OR**
3. The patient is unable to receive or has a clinical contraindication to conventional therapy (e.g., corticosteroids, 5-aminosalicylate, azathioprine, 6-mercaptopurine, metronidazole, methotrexate).

Coverage is provided for **Pediatric Crohn’s Disease** if:
1. Patient is a child (≥ 6 years of age) with moderately to severely active Crohn’s disease, **AND**
2. The patient has experienced a therapeutic failure or inadequate response to conventional therapy (e.g., corticosteroids, 5-aminosalicylate, azathioprine, 6-mercaptopurine, metronidazole, methotrexate); **OR**
3. The patient is unable to receive or has a clinical contraindication to conventional therapy (e.g., corticosteroids, 5-aminosalicylate, azathioprine, 6-mercaptopurine, metronidazole, methotrexate).

Coverage is provided for **Ulcerative Colitis** if:
1. Patient is an adult (≥ 18 years of age) with moderately to severely active ulcerative colitis, **AND**
2. The patient has experienced a therapeutic failure or inadequate response to conventional therapy (e.g., corticosteroids, 5-aminosalicylate, azathioprine, 6-mercaptopurine, metronidazole, methotrexate); **OR**
3. The patient is unable to receive or has a clinical contraindication to conventional therapy (e.g., corticosteroids, 5-aminosalicylate, azathioprine, 6-mercaptopurine, metronidazole, methotrexate).

Coverage is provided for **Rheumatoid Arthritis** if:
1. Patient is an adult (≥ 18 years of age) with moderately to severely active rheumatoid arthritis, **AND**
2. The patient has experienced a therapeutic failure or inadequate response to methotrexate; **OR**
3. The patient is unable to receive methotrexate or has a clinical contraindication to methotrexate.

Coverage is provided for **Psoriatic Arthritis** if:
1. Patient is an adult (≥ 18 years of age) with active psoriatic arthritis; **AND**
2. The patient has experienced a therapeutic failure or inadequate response to methotrexate; **OR**
3. The patient is unable to receive methotrexate or has a clinical contraindication to methotrexate.
Coverage is provided for **Polyarticular Juvenile Idiopathic Arthritis in patients aged 2 years or older** if:

1. Patient is ≥ 2 years of age and has moderately to severely active polyarticular juvenile idiopathic arthritis, **AND**
2. The patient has experienced a therapeutic failure or inadequate response to methotrexate; **OR**
3. The patient is unable to receive methotrexate or has a clinical contraindication to methotrexate.

Coverage is provided for **Plaque Psoriasis** if:

1. Patient is an adult (≥ 18 years of age) with moderate to severe chronic plaque psoriasis, **AND**
2. Patient is being managed by a dermatologist, **AND**
3. The patient is being managed by a dermatologist; **AND**
4. The patient has Body Surface Area (BSA) involvement of at least 5%; **OR**
5. The patient has involvement of the palms, soles, head and neck, or genitalia, causing disruption in normal daily activities and/or employment; **AND**
6. The patient has tried and failed, is intolerant to, or has a clinical contraindication to systemic therapy (methotrexate (oral or IM), cyclosporine, or acitretin); **OR**
7. The patient has tried and failed, is intolerant to, or has a clinical contraindication to phototherapy.

Coverage is NOT provided if:

1. Patient is using Humira in combination with other biologic agents including Enbrel, Stelara, Simponi, Remicade, Actemra, Kineret, Cimzia, Xeljanz, Orencia, Entyvio, Tysabri, or Rituxan.
2. Once-weekly doses of Humira are used in combination with methotrexate.

**QUANTITY LIMITATIONS**

**Rheumatoid Arthritis, Psoriatic Arthritis, Juvenile Idiopathic Arthritis, Ulcerative Colitis, Adult and Pediatric Crohn’s Disease, Ankylosing Spondylitis, and Plaque Psoriasis**

- The allowed quantity for maintenance doses of Humira is two 40 mg injections every 28 days.
- For patients with rheumatoid arthritis who are not taking concurrent methotrexate, four 40 mg injections every 28 days are allowed.

**Hidradenitis Suppurativa**

- The allowed quantity for maintenance dose is four 40 mg injections every 28 days.

**Refer to quantity limit chart on page 4**
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Quantity Limit</th>
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<tbody>
<tr>
<td>Rheumatoid Arthritis</td>
<td>40 mg every other week; some patients with RA not receiving methotrexate may benefit from increasing the frequency to 40 mg every week</td>
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<tr>
<td>Psoriatic Arthritis</td>
<td>40 mg every other week</td>
</tr>
<tr>
<td>Ankylosing Spondylitis</td>
<td>40 mg every other week</td>
</tr>
<tr>
<td>Plaque Psoriasis</td>
<td>Starting dose: 80 mg; followed by 40 mg every other week starting one week after initial dose</td>
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</tbody>
</table>
| Juvenile Idiopathic Arthritis   | • 10 kg (22 lbs) to < 15 kg (33 lbs): 10 mg every other week  
• 15 kg (33 lbs) to < 30 kg (66 lbs): 20 mg every other week  
• ≥ 30 kg (66 lbs): 40 mg every other week                          |
| Ulcerative Colitis              | • Initial dose (Day 1): 160 mg (four 40 mg injections in one day or two 40 mg injections per day for two consecutive days)  
• Second dose two weeks later (Day 15): 80 mg  
• Two weeks later (Day 29): Begin a maintenance dose of 40 mg every other week. |
| Adult Crohn’s Disease           | • Initial dose (Day 1): 160 mg (four 40 mg injections in one day or two 40 mg injections per day for two consecutive days)  
• Second dose two weeks later (Day 15): 80 mg  
• Two weeks later (Day 29): Begin a maintenance dose of 40 mg every other week. |
| Pediatric Crohn’s Disease       | • 17 kg (37 lbs) to < 40 kg (88 lbs): Initial dose (Day 1): 80mg (two 40 mg injection in one day); Second dose two weeks later (Day 15): 40 mg; two weeks later (Day 29): begin a maintenance dose of 20 mg every other week.  
• ≥ 40 kg (88 lbs): Initial dose (Day 1): 160mg (four 40 mg injection in one day or two 40 mg injections per day for two consecutive days); Second dose two weeks later (Day 15): 80 mg (two 40 mg injections in one day); two weeks later (Day 29): begin a maintenance dose of 40 mg every other week. |
| Hidradenitis Suppurativa        | • Initial dose (Day 1): 160 mg (given as four 40 mg injections on Day 1 or as two 40 mg injections per day on Days 1 and 2)  
• Second dose two weeks later (Day 15): 80 mg (two 40 mg injections in one day)  
• Third (Day 29) and subsequent doses: 40 mg every week. |
BLACK BOX WARNING: SERIOUS INFECTIONS AND MALIGNANCY

- Increased risk of serious infections leading to hospitalization or death, including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens.
- Discontinue Humira if a patient develops a serious infection or sepsis during treatment.
- Perform test for latent TB; if positive, start treatment for TB prior to starting Humira.
- Monitor all patients for active TB during treatment, even if initial latent TB test is negative.
- Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers including Humira.
- Post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have occurred in adolescent and young adults with inflammatory bowel disease treated with TNF blockers including Humira.

*See full prescribing information for complete boxed warning*

WARNINGS, PRECAUTIONS, AND CONTRAINDICATIONS

Contraindication: None

Warnings and Precautions:
- **Serious infections:** Do not start Humira during an active infection. If an infection develops, monitor carefully, and stop Humira if infection becomes serious.
- **Invasive fungal infections:** For patients who develop a systemic illness on Humira, consider empiric antifungal therapy for those who reside or travel to regions where mycoses are endemic.
- **Malignancies:** Incidence of malignancies was greater in Humira-treated patients than in controls.
- **Anaphylaxis or serious allergic reactions** may occur.
- **Hepatitis B virus reactivation:** Monitor HBV carriers during and several months after therapy. If reactivation occurs, stop Humira and begin anti-viral therapy.
- **Demyelinating disease:** Exacerbation or new onset, may occur.
- **Cytopenias, pancytopenia:** Advise patients to seek immediate medical attention if symptoms develop, and consider stopping Humira.
- **Heart failure:** Worsening or new onset, may occur.
- **Lupus-like syndrome:** Stop Humira if syndrome develops.

*See full prescribing information for complete warnings, precautions, and contraindications*

DOSAGE AND ADMINISTRATION

Humira is administered by subcutaneous injection.
- For the treatment of **Rheumatoid Arthritis and Psoriatic Arthritis**, 40 mg every other week. Some patients with rheumatoid arthritis not receiving methotrexate may benefit from increasing the frequency to 40 mg every week.
- For the treatment of **Juvenile Idiopathic Arthritis**,
  - 10 kg (22 lbs) to < 15 kg (33 lbs): 10 mg every other week.
  - 15 kg (33 lbs) to < 30 kg (66 lbs): 20 mg every other week.
  - ≥ 30 kg (66 lbs): 40 mg every other week.
- For the treatment of **Plaque Psoriasis**, 80 mg initial dose, followed by 40 mg every other week starting one week after initial dose.
- For the treatment of **Ankylosing Spondylitis**, 40 mg every other week.
- For the treatment of adults with **Crohn’s Disease and Ulcerative Colitis**, Initial dose (Day 1): 160 mg (four 40 mg injections in one day or two 40 mg injections per day for two consecutive days). Second dose two weeks later (Day 15): 80 mg. Two weeks later (Day 29): Begin a maintenance dose of 40 mg every other week. For patients with Ulcerative Colitis only: Only continue adalimumab in patients who have shown evidence of clinical remission by eight weeks (Day 57) of therapy.
- For the treatment of **Pediatric Crohn’s Disease**,  
  - 17 kg (37 lbs) to < 40 kg (88 lbs): Initial dose (Day 1): 80 mg (two 40 mg injection in one day); Second dose two weeks later (Day 15): 40 mg; two weeks later (Day 29): begin a maintenance dose of 20 mg every other week.  
  - ≥ 40 kg (88 lbs): Initial dose (Day 1): 160 mg (four 40 mg injection in one day or two 40 mg injections per day for two consecutive days); Second dose two weeks later (Day 15): 80 mg (two 40 mg injections in one day); two weeks later (Day 29): begin a maintenance dose of 40 mg every other week.  
- For the treatment of **Hidradenitis Suppurativa**,  
  - Initial dose (Day 1): 160 mg (given as four 40 mg injections on Day 1 or as two 40 mg injections per day on Days 1 and 2)  
  - Second dose two weeks later (Day 15): 80 mg (two 40 mg injections in one day)  
  - Third (Day 29) and subsequent doses: 40 mg every week.

**REFERENCES**


**POLICY IMPLEMENTATION/UPDATE INFORMATION**

- September 2015: Updated criteria under “Coverage is provided for Moderate to Severe Plaque Psoriasis”. The intent of the criteria is if phototherapy is unavailable to the patient, then the patient would need to meet the criteria for Stelara by try/fail/clinical contraindication to systemic therapy. The patient has been treated with phototherapy, unless the patient is not a candidate for phototherapy or phototherapy is not available to the patient. Revised to: The patient has tried and failed, is intolerant to, or has a clinical contraindication to phototherapy.
- September 2015: Added new FDA indication for Humira in the policy: Humira is indicated for the treatment of adult patients with moderate to severe hidradenitis suppurativa.