Clinical Policy: Adalimumab (Humira)

Reference Number: PA.CP.PHAR.242
Effective Date: 01/18
Last Review Date 04/18 Revision Log

Coding Implications

Description
Adalimumab (Humira®) is tumor necrosis factor (TNF) blocker.

FDA Approved Indication(s)
Humira is indicated for the treatment of

- Rheumatoid arthritis (RA): 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 RA
- Juvenile idiopathic arthritis (JIA): Reducing signs and symptoms of moderately to severely active polyarticular JIA in patients 2 years of age and older.
- Psoriatic arthritis (PsA): Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active PsA.
- Ankylosing spondylitis (AS): Reducing signs and symptoms in adult patients with active AS.
- Adult Crohn's disease (CD): Reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active CD who have had an inadequate response to conventional therapy. Reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab.
- Pediatric CD: Reducing signs and symptoms and inducing and maintaining clinical remission in patients 6 years of age and older with moderately to severely active CD who have had an inadequate response to corticosteroids or immunomodulators such as azathioprine, 6-mercaptopurine, or methotrexate.
- Ulcerative colitis (UC): 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).
- Plaque psoriasis (PsO): The 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.
- Hidradenitis suppurativa (HS): The treatment of moderate to severe hidradenitis suppurativa.
- Uveitis (UV): The treatment of non-infectious intermediate, posterior and panuveitis in adult patients.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of Pennsylvania Health and Wellness® that Humira is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Rheumatoid Arthritis (must meet all)**:**

1. Diagnosis of RA per American College of Rheumatology (ACR) criteria (refer to *Appendix B*);
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of methotrexate (MTX) for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effects are experienced;
   b. If intolerance or contraindication to MTX, failure of sulfasalazine, leflunomide, or hydroxychloroquine for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 40 mg every other week.

Approval duration: 6 months

B. Polyarticular Juvenile Idiopathic Arthritis (must meet all)**:**

1. Diagnosis of PJIA;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 2 years;
4. Member meets one of the following (a or b):
   a. Failure of MTX for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effects are experienced;
   b. If intolerance or contraindication to MTX, failure of sulfasalazine or leflunomide for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed the following:
   a. 10 kg (22 lbs) to <15 kg (33 lbs): 10 mg every other week
   b. 15 kg (33 lbs) to < 30 kg (66 lbs): 20 mg every other week
   c. ≥ 30 kg (66 lbs): 40 mg every other week.

Approval duration: 6 months

C. Psoriatic Arthritis (must meet all)**:**

1. Diagnosis of active PsA;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of MTX at up to maximally indicated doses, unless member has predominantly axial disease, contraindicated, or clinically significant adverse effects are experienced;
   b. If intolerance or contraindication to MTX (*see Appendix C*), failure of a ≥ 3 consecutive month trial of cyclosporine, sulfasalazine, or leflunomide at up to

maximally indicated doses, unless member has predominantly axial disease, contraindicated or clinically significant adverse effect are experienced;

5. For predominantly axial disease, failure of a ≥ 4-week trial of non-steroidal anti-inflammatory drugs (NSAIDs) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 40 mg every other week.

Approval duration: 6 months

D. Ankylosing Spondylitis (must meet all)**:**

1. Diagnosis of active AS;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;
4. Failure of at least TWO non-steroidal anti-inflammatory drugs (NSAIDs) at up to maximally indicated doses, each used for ≥ 4 weeks unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 40 mg every other week.

Approval duration: 6 months

E. Crohn's Disease (must meet all)**:**

1. Diagnosis of CD
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 6 years;
4. Failure of a ≥ 3 consecutive month trial of at least ONE immunomodulator (e.g., azathioprine, 6-MP, MTX) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed the following (a or b):
   a. Adults:
      i. Initial dose (Day 1): 160 mg
      ii. Second dose (Day 15): 80 mg
      iii. Maintenance dose (Day 29): 40 mg every other week
   b. Pediatrics:
      i. 17 kg (37 lbs.) to < 40 kg (88 lbs.): initial dose (Day 1): 80 mg; second dose (Day 15): 40 mg; maintenance (Day 29): 20 mg every other week;
      ii. ≥ 40 kg (88 lbs): initial dose (Day 1): 160 mg; second dose (Day 15): 80 mg; maintenance (Day 29): 40 mg every other week.

Approval duration: 6 months

F. Ulcerative Colitis (must meet all)**:**

1. Diagnosis of UC;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 18 years;
4. Failure of a ≥ 3 consecutive month trial of azathioprine, 6-MP, or an aminosalicylate (e.g., sulfasalazine) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed the following:

i. Initial dose (Day 1): 160 mg
ii. Second dose (Day 15): 80 mg
iii. Maintenance dose (Day 29): 40 mg every other week

Approval duration: 3 months

G. Plaque Psoriasis (must meet all)**:**

1. Diagnosis of PsO;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of MTX at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. If intolerance or contraindication to MTX (*see Appendix C*), failure of a ≥ 3 consecutive month trial of cyclosporine or acitretin at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 80 mg initial dose, followed by 40 mg every other week starting one week after initial dose.

Approval duration: 6 months

H. Hidradenitis Suppurativa (must meet all)**:**

1. Diagnosis of moderate to severe HS
2. Prescribed by or in consultation with a dermatologist, rheumatologist, or GI specialist;
3. Age ≥ 18 years;
4. Documentation of Hurley stage II or stage III;
5. Failure of a ≥ 3 consecutive month trial of systemic antibiotic therapy (e.g., clindamycin, minocycline, doxycycline, rifampin) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed the following:
   a. Initial dose (Day 1): 160 mg;
   b. Second dose (Day 15): 80 mg;
   c. Maintenance dose (Day 29): 40 mg every week.

Approval duration: 6 months

I. Uveitis (must meet all)**:**

1. Diagnosis of non-infectious intermediate, posterior or panuveitis;
2. Prescribed by or in consultation with an ophthalmologist;
3. Age ≥ 18 years;
4. Failure of a ≥ 2 week trial of a systemic corticosteroid (e.g., prednisone) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of a trial of a non-biologic immunosuppressive therapy (e.g., azathioprine, methotrexate, mycophenolate mofetil, cyclosporine, tacrolimus, cyclophosphamide,

chlorambucil) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 80 mg initial dose, followed by 40 mg every other week starting one week after initial dose.

Approval duration: 6 months

J. Other diagnoses/indications
1. Refer to PA.CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or Continuity of Care policy applies;
2. Member is responding positively to therapy (examples: sign/symptom reduction, no disease progression, no significant toxicity);
3. If request is for a dose increase, new dose does not exceed:
    a. RA (i or ii):
        i. 40 mg every other week;
        ii. 40 mg every week, if documentation supports inadequate response to a ≥ 3 month trial of 40 mg every other week or member is not a candidate for concurrent methotrexate and Humira due to contraindications or intolerance;
    b. For HS: 40 mg every week;
    c. For PJIA, CD, UC, PsA, AS, PsO, uveitis: 40 mg every other week.

Approval duration: 12 months

B. Other diagnoses/indications (1 or 2)**:**
1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or Continuity of Care policy applies.

Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to PA.CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to PA.CP.PHAR.57 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AS: ankylosing spondylitis
CCP: Crohn's disease
CRP: C-reactive protein
DMARD: disease-modifying antirheumatic drug
ESR: erythrocyte sedimentation rate

MTX: methotrexate
PJIA: polyarticular juvenile idiopathic arthritis
PsA: psoriatic arthritis
PsO: psoriasis
RA: rheumatoid arthritis
SC: subcutaneous
TB: tuberculosis
TNF: tumor necrosis factor
UC: ulcerative colitis

Appendix B: The 2010 ACR Classification Criteria for RA
Add score of categories A through D; a score of ≥ 6 out of 10 is needed for classification of a patient as having definite RA.

A	**Joint involvement**	Score
	1 large joint	0
	2-10 large joints	1
	1-3 small joints (with or without involvement of large joints)	2
	4-10 small joints (with or without involvement of large joints)	3
	> 10 joints (at least one small joint)	5
B	**Serology (at least one test result is needed for classification)**	
	Negative rheumatoid factor (RF) *and* negative anti-citrullinated protein antibody (ACPA)	0
	Low positive RF *or* low positive ACPA * *Low: < 3 x upper limit of normal*	2
	High positive RF *or* high positive ACPA * *High: ≥ 3 x upper limit of normal*	3
C	**Acute phase reactants (at least one test result is needed for classification)**	
	Normal C-reactive protein (CRP) and normal erythrocyte sedimentation rate (ESR)	0
	Abnormal CRP or normal ESR	1
D	**Duration of symptoms**	
	< 6 weeks	0
	≥ 6 weeks	1

Appendix C: Definition of MTX or DMARD Failure
- Definition of failure of MTX or DMARDs
  - Failure of a trial of conventional DMARDs:
    - In RA, failure of MTX or DMARD is defined as < 50% decrease in swollen joint count, < 50% decrease in tender joint count, and < 50% decrease in ESR, or < 50% decrease in CRP.
    - Child-bearing age is not considered a contraindication for use of MTX. Each drug has risks in pregnancy. An educated patient and family planning would allow use of MTX in patients who have no intention of immediate pregnancy.
    - Social use of alcohol is not considered a contraindication for use of MTX. MTX may only be contraindicated if patients choose to drink over 14 units of alcohol per week. However, excessive alcohol drinking can lead to worsening of the condition, so patients who are serious about clinical response to therapy should refrain from excessive alcohol consumption.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
RA, PsA, AS	• 40 mg every other week • Some patients with RA not receiving methotrexate may benefit from increasing the frequency to 40 mg every week.	40 mg every week
PJIA	• 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	40 mg every other week
Adult CD and UC	• Initial dose (Day 1): 160 mg • Second dose two weeks later (Day 15): 80 mg • Two weeks later (Day 29): Begin a maintenance dose of 40 mg every other week • UC only: Only continue Humira in patients who have shown evidence of clinical remission by 8 weeks (Day 57) of therapy.	40 mg every other week
Pediatric CD	17 kg (37 lbs) to < 40 kg (88 lbs): • Initial dose (Day 1): 80 mg • 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 • Second dose two weeks later (Day 15): 80 mg. • Two weeks later (Day 29): Begin maintenance dose of 20 mg every other week.	20 mg every other week
PsO or Uveitus	• Initial dose 80 mg, • One week after initial dose, 40 mg every other week	40 mg every other week
HS	• Initial dose (Day 1): 160 mg • Second dose two weeks later (Day 15): 80 mg • Third (Day 29) and subsequent doses: 40 mg every week	40 mg every week

VI. Product Availability

- 80 mg/0.8 mL in a single-use prefilled pen (HUMIRA Pen)
- 80 mg/0.8 mL in a single-use prefilled glass syringe
- 40 mg/0.8 mL in a single prefilled pen (HUMIRA Pen)
- 40 mg/0.4 mL in a single-use prefilled pen (HUMIRA Pen)
- 40 mg/0.8 mL in a single-use prefilled glass syringe
- 40 mg/0.4 mL in a single-use prefilled glass syringe
- 20 mg/0.4 mL in a single-use prefilled glass syringe
- 20 mg/0.2 mL in a single-use prefilled glass syringe
- 10 mg/0.2 mL in a single-use prefilled glass syringe
- 10 mg/0.1 mL in a single-use prefilled glass syringe

- 40 mg/0.8 mL in a single-use glass vial for institutional use only

VII. References

1. Humira Prescribing Information. North Chicago, IL: AbbVie, Inc.; May 2017. Available at http://www.rxabbvie.com/pdf/humira.pdf. Accessed February 27, 2018.
2. Smolen JS, Landewé R, Breedveld FC, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. *Ann Rheum Dis*. 2014; 73:492-509.
3. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. *Arthritis Care Res.* 2012; 64(5):625-639.
4. Ringold, S, Weiss PF, et al. 2013 Update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis. *Arthritis Care Res.* 2013; 65(10):2499-2512.
5. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res.* 2011; 63(4):465-482.
6. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011; 65(1):137-174.
7. Menter A, Gottlieb A, Feldman SR, et al. Guidelines for the management of psoriasis and psoriatic arthritis. Section 1: Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. *J Am Acad Dermatol.* 2008; 58(5):826-850.
8. Ward MM, Deodhar A, Aki EA, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol.* 2015. DOI 10.1002/ART.39298.
9. Braun J, van den berg R, et al. 2010 Update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Am Rheu Dis*. 2011; 70:896-904.
10. Lichtenstein GR, Hanauer SB, Sandborn WJ, and the Practice Parameters Committee of the American College of Gastroenterology. Management of Crohn's disease in adults. *Am J Gastroenterol.* 2009; 104(2):465-483.
11. Kornbluth A, Sachar DB. Ulcerative Colitis Practice Guidelines in Adults: American College of Gastroenterology, Practice Parameters Committee. *Am J Gastroenterol.* 2010; 105:501-523.
12. Zouboulis CC, Desai N, Emtestam L, et al. European S1 guideline for the treatment of hidradenitis suppurativa/acne inversa. *J Eur Acad Dermatol Venereol*. April 2015; 29(4):619-44. Epub 2015 Jan 30.
13. Levy-Clarke G, Jabs DA, Read RW, et al. Expert panel recommendations for the use of anti-tumor necrosis factor biologic agents in patients with ocular inflammatory disorders. *Ophthalmology.* 2014; 121:785.

14. Gulliver W, Zouboulis CC, Prens E, et al. Evidence-based approach to the treatment of hidradenitis suppurative/acne inversa, based on the European guidelines for hidradenitis suppurativa. *Rev Endocr Metab Disord*. February 1, 2016. DOI 10.1007/s11154-016-9328-5.
15. Zouboulis, CC. Adalimumab for the treatment of hidradenitis suppurativa/acne inversa. *Expert Review of Clinical Immunology*. August 29, 2016. DOI: 10.1080/1744666X.2016.1221762. Available at http://dx.doi.org/10.1080/1744666X.2016.1221762.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0135	Injection, adalimumab, 20 mg

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2018 annual review: removed TB testing requirement from all criteria, modified trial and failure for RA to at least one conventional DMARD, removed requirements for specific criteria relating to diagnosis for CD and PsO, modified gastroenterologist specialty requirement to gastrointestinal specialist for CD/UC, added aminosalicylate as an option for trial and failure for UC, removed trial and failure of phototherapy and topical therapy for PsO, modified trial and failure for PsO to require methotrexate (or another agent if methotrexate is not tolerated or contraindicated, generalized trial of failure of systemic antibiotics for HS, added rheumatologist as an option for specialist requirement for UV, modified trial and failure for UV to require both systemic corticosteroid and immunosuppressive therapy; references reviewed and updated.	2.27.18	