Clinical Policy: Adalimumab (Humira), Adalimumab-atto (Amjevita), Adalimumab-adbm (Cyltezo), Adalimumab-bwwd (Hadlima), Adalimumab-adaz (Hyrimoz)

Reference Number: CP.PHAR.242
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Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Adalimumab (Humira®), adalimumab-atto (Amjevita™), adalimumab-adbm (Cyltezo™), adalimumab-bwwd (Hadlima™), and adalimumab-adaz (Hyrimoz™) are tumor necrosis factor (TNF) blockers.

FDA Approved Indication(s)

Indications	Description	Humira	Amjevita, Cyltezo, Hadilma, Hyrimoz
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	X	X
Juvenile idiopathic arthritis (JIA)	Reducing signs and symptoms of moderately to severely active polyarticular JIA (PJIA) in patients 2 (Humira) or 4 (Amjevita) years of age and older	X	X
Psoriatic arthritis (PsA)	Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active PsA	X	X
Ankylosing spondylitis (AS)	Reducing signs and symptoms in adult patients with active AS	X	X
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 (products)	X	X
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	X	–

Indications	Description	Humira	Amjevita, Cyltezo, Hadilma, Hyrimoz
	CD who have had an inadequate response to corticosteroids or immunomodulators such as azathioprine, 6-mercaptopurine, or methotrexate (MTX)		
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). The effectiveness of adalimumab products has not been established in patients who have lost response to or were intolerant to TNF blockers	X	X
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	X	X
Hidradenitis suppurativa (HS)	The treatment of moderate to severe hidradenitis suppurativa in patients 12 years of age and older	X	–
Uveitis (UV)	The treatment of non-infectious intermediate, posterior and panuveitis in adults and pediatric patients 2 years of age and older	X	–

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Humira, Amjevita, Cyltezo, and Hadlima are **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 (*see Appendix G*);
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 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 D*), failure of a ≥ 3 consecutive month trial of at least ONE conventional disease-modifying antirheumatic drug [DMARD] (e.g., sulfasalazine, leflunomide, hydroxychloroquine) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

5. Failure of at least TWO of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Enbrel®, Kevzara®, Xeljanz®/Xeljanz XR®;
   **Prior authorization is required for Enbrel, Kevzara, and Xeljanz/Xeljanz XR*
6. Documentation of baseline clinical disease activity index (CDAI) score (*see Appendix H*);
7. 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 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 D*), failure of a ≥ 3 consecutive month trial of sulfasalazine or leflunomide at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of ≥ 3 consecutive months trial of Enbrel, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for Enbrel*
6. Dose does not exceed one of the following (a, b, or c):
   a. Weight 10 kg (22 lbs) to <15 kg (33 lbs): 10 mg every other week;
   b. Weight 15 kg (33 lbs) to < 30 kg (66 lbs): 20 mg every other week;
   c. Weight ≥ 30 kg (66 lbs): 40 mg every other week.

Approval duration: 6 months

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

1. Diagnosis of PsA;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 18 years;
4. Failure of at least THREE of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Enbrel®, Otezla®, Simponi®/Simponi Aria®, Taltz®, Xeljanz®/Xeljanz XR®;
   **Prior authorization is required for Enbrel, Otezla, Simponi/Simponi Aria, Taltz, Xeljanz/Xeljanz XR*
5. Dose does not exceed 40 mg every other week.

Approval duration: 6 months

D. Ankylosing Spondylitis (must meet all)**:**
1. Diagnosis of AS;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;
4. Failure of at least TWO NSAIDs at up to maximally indicated doses, each used for ≥ 4 weeks unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of at least TWO of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Cimzia®, Enbrel, Taltz;
   **Prior authorization is required for Cimzia, Enbrel, and Taltz*
6. 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. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of at least ONE immunomodulator (e.g., azathioprine, 6-mercaptopurine [6-MP], MTX) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. Medical justification supports inability to use immunomodulators (*see Appendix E*);
5. Dose does not exceed one of the following (a or b):
   a. Adults: 160 mg on Day 1 and 80 mg on Day 15, followed by maintenance dose of 40 mg every other week starting Day 29;
   b. Pediatrics (i or ii):
      i. Weight 17 kg (37 lbs.) to < 40 kg (88 lbs.): 80 mg on Day 1 and 40 mg on Day 15, followed by maintenance dose of 20 mg every other week starting Day 29;
      ii. Weight ≥ 40 kg (88 lbs): 160 mg on Day 1 and 80 mg on Day 15, followed by maintenance dose of 40 mg every other week starting Day 29.

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. Documentation of a Mayo Score ≥ 6 (*see Appendix F*);
5. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 160 mg on Day 1 and 80 mg on Day 15, followed by maintenance dose of 40 mg every other week starting Day 29.

Approval duration: 6 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 D*), 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. Failure of a ≥ 3 consecutive month trial of Taltz, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for Taltz*
6. Dose does not exceed 80 mg initial dose, followed by maintenance dose of 40 mg every other week starting one week after initial dose.

Approval duration: 6 months

H. Hidradenitis Suppurativa (must meet all)**:**
1. Diagnosis of HS;
2. Prescribed by or in consultation with a dermatologist, rheumatologist, or gastroenterologist;
3. Age ≥ 12 years;
4. Documentation of Hurley stage II or stage III (*see Appendix D*);
5. Failure of a ≥ 3 consecutive month trial of TWO of the following at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced:
   a. Systemic antibiotic therapy (e.g., clindamycin, minocycline, doxycycline, rifampin);
   b. Oral retinoids;
   c. Hormonal treatment;
6. Dose does not exceed 160 mg on Day 1 and 80 mg on Day 15, followed by maintenance dose of 40 mg every week starting Day 29.

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 or rheumatologist;
3. Age ≥ 2 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 maintenance dose of 40 mg every other week starting one week after initial dose.

Approval duration: 6 months

J. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Rheumatoid Arthritis (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by a decrease in CDAI score since baseline (*see Appendix H*);
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):*
   a. 40 mg every other week;
   b. 40 mg every week and both of the following (i and ii):
      i. 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;
      ii. Failure of ALL of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Enbrel®, Kevzara®, Xeljanz®/Xeljanz XR®.

Approval duration: 12 months*
**(If new dosing regimen, approve for 6 months)*

B. All Other Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member meets one of the following (a or b):
   a. For HS, at least a 25% reduction in inflammatory nodules and abscesses;
   b. For all other indications: member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. PJIA, PsA, AS, CD, UC, PsO, UV: 40 mg every other week;
   b. HS: 40 mg every week.

Approval duration: 12 months*
**(If new dosing regimen, approve for 6 months)*

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

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 the off label use policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

6-MP: 6-mercaptopurine
AS: ankylosing spondylitis
CD: Crohn's disease
CDAI: clinical disease activity index
DMARD: disease-modifying antirheumatic drug
FDA: Food and Drug Administration
GI: gastrointestinal
HS: hidradenitis suppurative
MTX: methotrexate
NSAIDs: nonsteroidal anti-inflammatory drugs
PJIA: polyarticular juvenile idiopathic arthritis
PsA: psoriatic arthritis
PsO: psoriasis
RA: rheumatoid arthritis
TNF: tumor necrosis factor
UC: ulcerative colitis
UV: uveitis

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
acitretin (Soriatane®)	**PsO, HS** 25 or 50 mg PO QD	50 mg/day
azathioprine (Azasan®, Imuran®)	**RA** 1 mg/kg/day PO QD or divided BID **CD*, UV*** 1.5 – 2 mg/kg/day PO	2.5 mg/kg/day
chlorambucil (Leukeran®)	**UV*** 0.2 mg/kg PO QD, then taper to 0.1 mg/kg PO QD or less	0.2 mg/kg/day
clindamycin (Cleocin®) + rifampin (Rifadin®)	**HS*** clindamycin 300 mg PO BID and rifampin 300 mg PO BID	clindamycin: 1,800 mg/day rifampin: 600 mg/day
corticosteroids	**CD*** prednisone 40 mg PO QD for 2 weeks or IV 50 – 100 mg Q6H for 1 week	Various

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	budesonide (Entocort EC®) 6 – 9 mg PO QD **UV*** prednisone 5 – 60 mg/day PO in 1 – 4 divided doses	
Cuprimine® (d-penicillamine)	**RA*** Initial dose: 125 or 250 mg PO QD Maintenance dose: 500 – 750 mg/day PO QD	1,500 mg/day
cyclophosphamide (Cytoxan®)	**UV*** 1 – 2 mg/kg/day PO	N/A
cyclosporine (Sandimmune®, Neoral®)	**PsO** 2.5 mg/kg/day PO divided BID **RA** 2.5 – 4 mg/kg/day PO divided BID **UV*** 2.5 – 5 mg/kg/day PO in divided doses	PsO, RA: 4 mg/kg/day UV: 5 mg/kg/day
doxycycline (Acticlate®)	**HS*** 50 – 100 mg PO BID	300 mg/day
Hormonal agents (e.g., estrogen-containing combined oral contraceptives, spironolactone)	**HS** varies	varies
hydroxychloroquine (Plaquenil®)	**RA*** Initial dose: 400 – 600 mg/day PO QD Maintenance dose: 200 – 400 mg/day PO QD	600 mg/day
Isotretinoin (Absorica®, Amnesteem®, Claravis®, Myorisan®, Zenatane®)	**HS** varies	varies 1.6 to 2 mg/kg/day
leflunomide (Arava®)	**PJIA*** Weight < 20 kg: 10 mg every other day PO Weight 20 - 40 kg: 10 mg/day PO Weight > 40 kg: 20 mg/day PO	20 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	RA 100 mg PO QD for 3 days, then 20 mg PO QD	
6-mercaptopurine (Purixan®)	**CD*** 50 mg PO QD or 1 – 2 mg/kg/day PO	2 mg/kg/day
methotrexate (Rheumatrex®)	**CD*** 15 – 25 mg/week IM or SC **PsO** 10 – 25 mg/week PO or 2.5 mg PO Q12 hr for 3 doses/week **PJIA*** 10 – 20 mg/m^2/week PO, SC, or IM **RA** 7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week **UV*** 7.5 – 20 mg/week PO	30 mg/week
minocycline (Minocin®)	**HS*** 50 – 100 mg PO BID	200 mg/day
mycophenolate mofetil (Cellcept®)	**UV*** 500 – 1,000 mg PO BID	3 g/day
NSAIDs (e.g., indomethacin, ibuprofen, naproxen, celecoxib)	**AS** Varies	Varies
Pentasa® (mesalamine)	**CD** 1,000 mg PO QID	4 g/day
Ridaura® (auranofin)	**RA** 6 mg PO QD or 3 mg PO BID	9 mg/day (3 mg TID)
sulfasalazine (Azulfidine®)	**PJIA*** 30-50 mg/kg/day PO divided BID **RA** 2 g/day PO in divided doses	PJIA: 2 g/day RA: 3 g/day UC: 4 g/day
tacrolimus (Prograf®)	**CD*** 0.27 mg/kg/day PO in divided doses or 0.15 – 0.29 mg/kg/day PO **UV***	N/A

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	0.1-0.15 mg/kg/day PO	
Enbrel® (etanercept)	**AS** 50 mg SC once weekly **PJIA** Weight < 63 kg: 0.8 mg/kg SC once weekly Weight ≥ 63 kg: 50 mg SC once weekly **PsA, RA** 25 mg SC twice weekly or 50 mg SC once weekly	50 mg/week
Cimzia® (certolizumab)	**AS** Initial dose: 400 mg SC at 0, 2, and 4 weeks Maintenance dose: 200 mg SC every other week (or 400 mg SC every 4 weeks)	400 mg every 4 weeks
Kevzara® (sarilumab)	**RA** 200 mg SC once every two weeks	200 mg/2 weeks
Otezla® (apremilast)	**PsA** Initial dose: Day 1: 10 mg PO QAM Day 2: 10 mg PO QAM and 10 mg PO QPM Day 3: 10 mg PO QAM and 20 mg PO QPM Day 4: 20 mg PO QAM and 20 mg PO QPM Day 5: 20 mg PO QAM and 30 mg PO QPM Maintenance dose: Day 6 and thereafter: 30 mg PO BID	60 mg/day
Simponi® (golimumab)	**PsA** 50 mg SC once monthly	50 mg/month
Simponi Aria® (golimumab)	**PsA** Initial dose: 2 mg/kg IV at weeks 0 and 4 Maintenance dose: 2 mg/kg IV every 8 weeks	2 mg/kg every 8 weeks

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Taltz® (ixekizumab)	**AS, PsA** Initial dose: 160 mg (two 80 mg injections) SC at week 0 Maintenance dose: 80 mg SC every 4 weeks **PsO** Initial dose: 160 mg (two 80 mg injections) SC at week 0, then 80 mg SC at weeks 2, 4, 6, 8, 10, and 12 Maintenance dose: 80 mg SC every 4 weeks	80 mg every 4 weeks
Xeljanz® (tofacitinib)	**PsA, RA** 5 mg PO BID	10 mg/day
Xeljanz XR® (tofacitinib extended-release)	**PsA, RA** 11 mg PO QD	11 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s):
  - Serious infections
  - Malignancy

Appendix D: General Information

- Definition of failure of MTX or DMARDs
  - 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.
- Examples of positive response to therapy may include, but are not limited to:
  - Reduction in joint pain/swelling/tenderness
  - Improvement in ESR/CRP levels
  - Improvements in activities of daily living
- Hidradenitis suppurativa:

  - HS is sometimes referred to as: "acne inversa, acne conglobata, apocrine acne, apocrinitis, Fox-den disease, hidradenitis axillaris, HS, pyodermia sinifica fistulans, Velpeau's disease, and Verneuil's disease."
  - In HS, Hurley stages are used to determine severity of disease. Hurley stage II indicates moderate disease, and is characterized by recurrent abscesses, with sinus tracts and scarring, presenting as single or multiple widely separated lesions. Hurley stage III indicates severe disease, and is characterized by diffuse or near-diffuse involvement presenting as multiple interconnected tracts and abscesses across an entire area.
- Ulcerative colitis: there is insufficient evidence to support the off-label weekly dosing of Humira for the treatment of moderate-to-severe UC. It is the position of Centene Corporation® that the off-label weekly dosing of Humira for the treatment of moderate-to-severe UC is investigational and not medically necessary at this time.
  - The evidence from the *post hoc* study of the Humira pivotal trial suggests further studies are needed to confirm the benefit of weekly Humira dosing for the treatment of UC in patients with inadequate or loss of therapeutic response to treatment with Humira every other week. No large, randomized or prospective studies have been published to support the efficacy of the higher frequency of dosing, while national and international treatment guidelines also do not strongly support dose escalation of Humira for UC. The current market consensus is that weekly dosing of Humira is not medically necessary due to lack of evidence to support its benefit.
- PsA: According to the 2018 American College of Rheumatology and National Psoriasis Foundation guidelines, TNF inhibitors or oral small molecules (e.g., methotrexate, sulfasalazine, cyclosporine, leflunomide, apremilast) are preferred over other biologics (e.g., interleukin-17 inhibitors or interleukin-12/23 inhibitors) for treatment-naïve disease. TNF inhibitors are also generally recommended over oral small molecules as first-line therapy unless disease is not severe, member prefers oral agents, or TNF inhibitor therapy is contraindicated.

Appendix E: Medical Justification

- The following may be considered for medical justification supporting inability to use an immunomodulator for Crohn's disease:
  - Inability to induce short-term symptomatic remission with a 3-month trial of systemic glucocorticoids
  - High-risk factors for intestinal complications may include:
    - Initial extensive ileal, ileocolonic, or proximal GI involvement
    - Initial extensive perianal/severe rectal disease
    - Fistulizing disease (e.g., perianal, enterocutaneous, and rectovaginal fistulas)
    - Deep ulcerations
    - Penetrating, stricturing or stenosis disease and/or phenotype
    - Intestinal obstruction or abscess
  - High risk factors for postoperative recurrence may include:
    - Less than 10 years duration between time of diagnosis and surgery
    - Disease location in the ileum and colon
    - Perianal fistula
    - Prior history of surgical resection

- Use of corticosteroids prior to surgery

Appendix F: Mayo Score

- Mayo Score: evaluates ulcerative colitis stage, based on four parameters: stool frequency, rectal bleeding, endoscopic evaluation and Physician's global assessment. Each parameter of the score ranges from zero (normal or inactive disease) to 3 (severe activity) with an overall score of 12.

Score	Decoding
0 – 2	Remission
3 – 5	Mild activity
6 – 10	Moderate activity
>10	Severe activity

- The following may be considered for medical justification supporting inability to use an immunomodulator for ulcerative colitis:
  - Documentation of Mayo Score 6 – 12 indicative of moderate to severe ulcerative colitis.

Appendix G: 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 H: Clinical Disease Activity Index (CDAI) Score

The Clinical Disease Activity Index (CDAI) is a composite index for assessing disease activity in RA. CDAI is based on the simple summation of the count of swollen/tender joint

count of 28 joints along with patient and physician global assessment on VAS (0–10 cm) Scale for estimating disease activity. The CDAI score ranges from 0 to 76.

CDAI Score	Disease state interpretation
≤ 2.8	Remission
2.8 to ≤ 10	Low disease activity
10 to ≤ 22	Moderate disease activity
> 22	High disease activity

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
RA	40 mg SC every other week Some patients with RA not receiving concomitant methotrexate may benefit from increasing the frequency to 40 mg every week.	40 mg/week
PJIA	Weight 10 kg (22 lbs) to < 15 kg (33 lbs): 10 mg SC every other week Weight 15 kg (33 lbs) to < 30 kg (66 lbs): 20 mg SC every other week Weight ≥ 30 kg (66 lbs): 40 mg SC every other week	40 mg every other week
PsA AS	40 mg SC every other week	40 mg every other week
CD	Initial dose: *Adults:* 160 mg SC on Day 1, then 80 mg SC on Day 15 *Pediatrics:* Weight 17 kg (37 lbs) to < 40 kg (88 lbs): 80 mg SC on Day 1, then 40 mg SC on Day 15 Weight ≥ 40 kg (88 lbs): 160 mg SC on Day 1, then 80 mg SC on Day 15 Maintenance dose: *Adults:* 40 mg SC every other week starting on Day 29 *Pediatrics:* Weight 17 kg (37 lbs) to < 40 kg (88 lbs): 20 mg SC every other week starting on Day 29 Weight ≥ 40 kg (88 lbs): 40 mg SC every other week starting on Day 29	40 mg every other week
UC	Initial dose: 160 mg SC on Day 1, then 80 mg SC on Day 15 Maintenance dose: 40 mg SC every other week starting on Day 29	40 mg every other week

Indication	Dosing Regimen	Maximum Dose
PsO	Initial dose: 80 mg SC Maintenance dose: 40 mg SC every other week starting one week after initial dose	40 mg every other week
UV	*Pediatrics:* Weight 10 kg (22 lbs) to < 15 kg (33 lbs): 10 mg SC every other week Weight 15 kg (33 lbs) to < 30 kg (66 lbs): 20 mg SC every other week Weight ≥ 30 kg (66 lbs): 40 mg SC every other week *Adults:* Initial dose of 80 mg SC, followed by 40 mg SC every other week starting one week after the initial dose	40 mg every other week
HS	*For patients 12 years of age and older weighing at least 30 kg:* Initial dose: Weight 30 kg (66 lbS) to < 60 kg (132 lbs): 80 mg SC on Day 1, then 40 mg on Day 8 Weight ≥ 60 kg (132 lbs): 160 mg SC on Day 1, then 80 mg SC on Day 15 Maintenance dose: Weight 30 kg (66 lbS) to < 60 kg (132 lbs): 40 mg every other week Weight ≥ 60 kg (132 lbs): 40 mg SC once weekly starting on Day 29	40 mg/week

VI. Product Availability

Drug Name	Availability
adalimumab (Humira)	• Single-dose prefilled pen: 80 mg/0.8 mL, 40 mg/0.8 mL, 40 mg/0.4 mL • Single-dose prefilled syringe: 80 mg/0.8 mL, 40 mg/0.8 mL, 40 mg/0.4 mL, 20 mg/0.4 mL, 20 mg/0.2 mL, 10 mg/0.2 mL, 10 mg/0.1 mL • Single-use vial for institutional use only: 40 mg/0.8 mL
Adalimumab-atto (Amjevita)	• Single-dose prefilled SureClick autoinjector: 40 mg/0.8 mL • Single-dose prefilled syringe: 40 mg/0.8 mL, 20 mg/0.4 mL
Adalimumab-adbm (Cyltezo)	• Single-dose prefilled syringe: 40 mg/0.8 mL, 20 mg/0.4 mL
Adalimumab-bwwd (Hadlima)	• Single-dose prefilled PushTouch autoinjector: 40 mg/0.8 mL • Single-dose prefilled syringe: 40 mg/0.8 mL

Drug Name	Availability
Adalimumab-adaz (Hyrimoz)	• Single-dose prefilled glass syringe (with BD UltraSafe Passive™ Needle Guard): 40 mg/0.8 mL • Single-dose prefilled pen (Sensoready® Pen): 40 mg/0.8 mL

VII. References

1. Humira Prescribing Information. North Chicago, IL: AbbVie, Inc.; January 2019. Available at: http://www.rxabbvie.com/pdf/humira.pdf. Accessed February 26, 2020.
2. Amjevita Prescribing Inormation. Thousand Oaks, CA: Amgen Inc.; June 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761024s004lbl.pdf. Accessed February 26, 2020.
3. Cyltezo Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; September 2019. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761058s003lbl.pdf. Accessed February 26, 2020.
4. Hadlima Prescribing Information. Whitehouse Station, NJ: Merck Sharp & Dohm Corp.; July 2019. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/761059s000lbl.pdf. Accessed February 26, 2020.
5. Hyrimoz Prescribing Information. Princeton, NJ: Sandoz Inc.; October 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761071lbl.pdf. Accessed April 27, 2020.

Rheumatoid Arthritis

6. 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.
7. 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.
8. 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.
9. 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.
10. Dhaon P, Das SK, Srivastava R, et al. Performances of clinical disease activity index (CDAI) and simplified disease activity index (SDAI) appear to be better than the gold standard disease assessment score (DAS-28-CRP) to assess ruehmatoid arthritis patients. Int J Rheum Dis. 2018; 21:1933-1939.
11. Aletaha D, Neogi T, Silman AJ, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum 2010; 62(9):2569-2581. DOI 10.1002/art.27584

Psoriasis and Psoriatic Arthritis

12. 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.
13. 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.
14. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. Ann Rheum Dis 2015;0:1-12. doi:10.1136/annrheumdis-2015-208337
15. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis. American College of Rheumatology. 2019; 71(1):5-32. doi: 10.1002/art.40726

Spondylitis

16. 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.
17. 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.

Crohn's Disease and Ulcerative Colitis

18. Lichtenstein GR, Loftus Jr. EV, Isaacs KI, Regueiro MD, Gerson LB, and Sands BE. ACG clinical guideline: management of Crohn's disease in adults. Am J Gastroenterol. 2018; 113:481-517.
19. Rubin DT,Ananthakrishnan AN, Siegel CA, et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol 2019;114:384-413

Hidradenitis Suppurativa

20. 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.
21. 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.
22. 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.
23. Alikhan A, Sayed C, Alavi A, et al. North American Clinical Management Guidelines for Hidradenitis Suppurativa: a publication from the United States and Canadian Hidradenitis Suppurativa Foundations. Part II: topical, intralesional, and systemic medical management. J Am Acad Dermatol. 2019; pii: S0190-9622(19)30368-8. doi: 10.1016/j.jaad.2019.02.068.

Uveitis

24. 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.

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	P&T Approval Date
Policy split from CP.PHAR.86.ArthritisTreatments, CP.PHAR.85.Psoriasis Treatments, CP.PHAR.87.IBD Treatment_4_ RA, PJIA, PsA, AS, CD, UC, PsO: Removed criteria related to HBV, malignant disease, concomitant use with other biologics, and concurrent administration of live vaccines; added dosing requirement. PJIA: removed question related to number of affected joints; modified criteria to require trial of MTX, unless contraindicated; added sulfasalazine as an alternative to MTX if MTX is contraindicated. RA: changed age requirement to 18 years per PI; modified criteria to require trial of MTX, unless contraindicated; added sulfasalazine as an alternative to MTX if MTX is contraindicated. PsO: removed duration of trial for topical and phototherapy. Re-auth: combined into All Indications; added dosing and reasons to discontinue; for PsO modified specific efficacy criteria related to Psoriasis Area and Severity Index (PASI)-75 to general efficacy statement. Modified approval duration to 6 months for initial and 12 months for renewal with the exception of UC which is 2 months (time to clinical remission per PI) and 12 months. HS: Added criteria for FDA labeled indication criteria. Uveitis: Added criteria for FDA labeled indication for uveitis. Shortened background section.	08.16	08.16
PsO: Removed Otezla from list of therapies to trial per PDL.	11.16	
Added requirement for supportive documentation for dose escalation for Humira for use in rheumatoid arthritis.	03.17	
Converted to new template. RA: Revised criteria for confirmation of RA diagnosis per 2010 ACR Criteria. CD: revised list of poor prognostic indicators per AGA guidelines, added examples of extensive disease. PsO: Trial requirement modified to require the concomitant use of oral and topical or phototherapy. Added initial dosing regimen for all indications where applicable. Safety criteria was applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs.	08.17	08.17
Added TB requirement for plaque psoriasis for consistency	09.22.17	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Typo removed from AS criteria to ensure prior of first line agent to align with other covered diagnosis	12.08.17	
2Q 2018 annual review: policies combined for HIM and Medicaid lines of business; Medicaid and HIM: 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; modified initial approval duration for UC from 3 months to 6 months; references reviewed and updated.	02.27.18	05.18
4Q 2018 annual review: updated pediatric indication expansion for uveitis and adolescent indication expansion for hidradenitis suppurativa; modified prescriber specialist from GI specialist to gastroenterologist for CD, UC, and HS; added trial and failure of immunosuppressants, or medical necessity for use of biologics in CD; allowed bypassing conventional DMARDs for axial PsA and required trial of NSAIDs; references reviewed and updated.	09.04.18	11.18
2Q 2019 annual review: removed trial and failure of conventional DMARDs (e.g., MTX)/NSAIDs for PsA per 2018 ACR/NPF guidelines; revised approval duration to 6 months if request is for continuation of therapy with a new (e.g., increased dose/frequency) regimen; references reviewed and updated.	03.05.19	05.19
RT4: no significant change; added biosimilar Amjevita to policy.	06.18.19	
RT4: no significant change; added biosimilars Cyltezo and Hadlima to policy.	09.23.19	
Removed HIM line of business; updated preferred redirections based on SDC recommendation and prior clinical guidance: for PsA, added redirection to 3 of 5 (Enbrel, Simponi, Talftz, Otezla, Xeljanz/Xeljanz XR); for PsO, added redirection to Taltz; for AS, added redirection to 2 of 3 (Enbrel, Cimzia, Taltz); for PJIA, added redirection to etanercept; for RA, added redirection to 2 of 3 (Enbrel, Kevzara, Xeljanz/Xeljanz XR) for initial therapy and 3 of 3 (Enbrel, Kevzara, Xeljanz/Xeljanz XR) for continued therapy at weekly dosing interval.	12.16.19	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2020 annual review: added Hyrimoz to the policy; for UC, revised redirection from AZA, 6-MP, and ASA to corticosteroids and added requirement of Mayoscore of at least 6; for RA, added specific diagnostic criteria for definite RA, baseline CDAI score requirement, and decrease in CDAI score as positive response to therapy; for HS, revised requirement from systemic antibiotics to additionally require oral retinoids or hormonal therapy, and required at least a 25% reduction in inflammatory nodules and abscesses for reauthorization; references reviewed and updated.	04.23.20	05.20

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.