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

Reference Number: IL.PHAR.242
Effective Date: 1.13.2020
Last Review Date: 2.20.23
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-afzb (Abrilada™), adalimumab-atto (Amjevita™), adalimumab-adbm (Cyltezo™), adalimumab-bwwd (Hadlima™), adalimumab-fkjp (Hulio®), adalimumab-adaz (Hyrimoz™), and adalimumab-aacf (Idacio®) are tumor necrosis factor (TNF) blockers.

FDA Approved Indication(s)

Indications	Description	Humira	Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, Hyrimoz, Idacio
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 in patients 2 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
Crohn's disease (CD)	Treatment of moderately to severely active CD in adults and pediatric patients 6 years of age and older	X	X
Adult ulcerative colitis (UC)	Treatment of moderately to severely active ulcerative colitis in adult patients	X	X

Indications	Description	Humira	Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, Hyrimoz, Idacio
	Limitation of use: Effectiveness has not been established in patients who have lost response to or were intolerant to TNF blockers		
Pediatric UC	Treatment of moderately to severely active UC in pediatric patients 5 years of age and older Limitation of use: Effectiveness has not been established in patients who have lost response to or were intolerant to TNF blockers	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, Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, Hyrimoz, and Idacio 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. Request is for Humira®
4. Age ≥ 18 years;
5. 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;

6. Documentation of one of the following baseline assessment scores (a or b):
   a. Clinical disease activity index (CDAI) score (*see Appendix H*);
   b. Routine assessment of patient index data 3 (RAPID3) score (*see Appendix I)*;

7. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
8. 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 as evidenced by ≥ 5 joints with active arthritis;
2. Prescribed by or in consultation with a rheumatologist;
3. Request is for Humira®
4. Age ≥ 2 years;
5. Documented baseline 10-joint clinical juvenile arthritis disease activity score (cJADAS-10) (*see Appendix J*);
6. Member meets one of the following (a, b, c, or d):
   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;
   c. For sacroiliitis/axial spine involvement (i.e., spine, hip), failure of a ≥ 4 week trial of an NSAID at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   d. Documented presence of high disease activity as evidenced by a cJADAS-10 > 8.5 (*see Appendix J*);
7. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
8. 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. Request is for Humira®
4. Age ≥ 18 years;
5. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
6. 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. Request is for Humira®
4. Age ≥ 18 years;
5. 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;
6. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
7. 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. Request is for Humira®
4. Age ≥ 6 years;
5. 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*);
6. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
7. 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. Request is for Humira®
4. Age ≥ 5 years;
5. Documentation of a Mayo Score ≥ 6 (*see Appendix F*);
6. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed one of the following (a, b, or c):
   a. For 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. For pediatric patients weighing more than 20 kg, but less than 40 kg: 80 mg on Day 1, 40 mg on Day 8 and Day 15, followed by maintenance doses of 40 mg every other week or 20 mg every week
   c. For pediatric patients weighing more than 40 kg: 160 mg on Day 1 and 80 mg on Day 8 and 15, followed by maintenance doses of 80 mg every other week or 40 mg every week.

Approval duration: 6 months

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

1. Diagnosis of moderate-to-severe PsO as evidenced by involvement of one of the following (a or b):
   a. ≥ 3% of total body surface area;
   b. Hands, feet, scalp, face, or genital area;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Request is for Humira®
4. Age ≥ 18 years;
5. Member meets one of the following (a, b or c):
   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 at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   c. Member has intolerance or contraindication to MTX and cyclosporine and failure of phototherapy, unless contraindicated or clinically significant adverse effects are experienced;

6. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
7. 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. Request is for Humira®
4. Age ≥ 12 years;
5. Documentation of Hurley stage II or stage III (*see Appendix D*);
6. Failure of at least One of the following for ≥ 3 consecutive months, at up to maximally indicated doses, unless clinically significant adverse effects are experienced, or all are contraindicated:
   a. Systemic antibiotic therapy (e.g., clindamycin, minocycline, doxycycline, rifampin);
   b. Oral retinoids (e.g., isotretinoin);
   c. Hormonal treatment (e.g., estrogen-containing combined oral contraceptives, spironolactone);
7. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
8. 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. Request is for Humira®
4. Age ≥ 2 years;
5. 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;
6. 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;
7. 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 (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the PDL (Medicaid), the no coverage criteria policy CP.PMN.255; or
   b. For drugs NOT on the PDL (Medicaid), the non-formulary policy: CP.PMN.16; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
   a. A decrease in CDAI (*see Appendix H*) or RAPID3 (*see Appendix I*) score from baseline;
   b. Medical justification stating inability to conduct CDAI re-assessment, and submission of RAPID3 score associated with disease severity that is similar to initial CDAI assessment or improved;
3. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
4. 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. Both of the following (i and ii):
      a. 40 mg every week (or 80 mg every other week);
      ii. 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;

Approval duration: 12 months*

**(If new dosing regimen, approve for 6 months)*

B. Other diagnoses/indications in Section I (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*

2. Member meets one of the following (a, b, or c):
   a. For HS, at least a 25% reduction in inflammatory nodules and abscesses;
   b. For pJIA, member is responding positively to therapy as evidenced by a decrease in cJADAS-10 from baseline (*see Appendix J*)
   c. For all other indications: member is responding positively to therapy;
3. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
4. If request is for a dose increase, new dose does not exceed one of the following (a, b, or c):
   a. PJIA, PsA, AS, CD, PsO, UV: 40 mg every other week;
   b. HS: 40 mg every week;
   c. For UC, one of the following (i or ii)
      i. 40 mg every other week or 20 mg every week;
      ii. 80 mg every other week or 40 mg every week, and member initiated Humira prior to 18 years of age.

Approval duration: 12 months*

**(If new dosing regimen, approve for 6 months)*

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy: CP.PMN.53 for Medicaid.
1. .

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.

B. Combination use of biological disease-modifying antirheumatic drugs (bDMARDs), including any tumor necrosis factor (TNF) antagonists [Cimzia®, Enbrel®, Simponi®, Avsola™, Inflectra™, Remicade®, Renflexis™], interleukin agents [Arcalyst® (IL-1 blocker), Ilaris® (IL-1 blocker), Kineret® (IL-1RA), Actemra® (IL-6RA), Kevzara® (IL-6RA), Stelara® (IL-12/23 inhibitor), Cosentyx® (IL-17A inhibitor), Taltz® (IL-17A

inhibitor), Siliq™ (IL-17RA), Ilumya™ (IL-23 inhibitor), Skyrizi™ (IL-23 inhibitor), Tremfya® (IL-23 inhibitor)], janus kinase inhibitors (JAKi) [Xeljanz®/Xeljanz® XR, Rinvoq™], anti-CD20 monoclonal antibodies [Rituxan®, Riabni™, Ruxience™, Truxima®, and Rituxan Hycela®], selective co-stimulation modulators [Orencia®], or integrin receptor antagonists [Entyvio®] because of the possibility of increased immunosuppression, neutropenia and increased risk of infection.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

6-MP: 6-mercaptopurine
AS: ankylosing spondylitis
CD: Crohn's disease
DMARD: disease-modifying antirheumatic drug
FDA: Food and Drug Administration
GI: gastrointestinal
HS: hidradenitis suppurative
CDAI: clinical disease activity index
cJADAS: clinical juvenile arthritis disease activity score
MTX: methotrexate
NSAIDs: nonsteroidal anti-inflammatory drugs
PJIA: polyarticular juvenile idiopathic arthritis
PsA: psoriatic arthritis
PsO: psoriasis
RA: rheumatoid arthritis
RAPID3: routine assessment of patient index data 3
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*, UC*, 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
hydroxychloroquine (Plaquenil®)	**RA*** Initial dose: 400 – 600 mg/day PO QD Maintenance dose: 200 – 400 mg/day PO QD	600 mg/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 **RA** 100 mg PO QD for 3 days, then 20 mg PO QD	20 mg/day
6-mercaptopurine (Purixan®)	**CD*** 50 mg PO QD or 1 – 2 mg/kg/day PO	2 mg/kg/day
methotrexate (Rheumatrex®)	**CD*, UC*** 15 – 25 mg/week IM or SC **PsO**	30 mg/week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	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	
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, UC** 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 **UC** <u>Initial dose:</u> 3 – 4 g/day PO in divided doses (not to exceed Q8 hrs) <u>Maintenance dose:</u> 2 g PO daily	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
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.

Appendix E: Immunomodulator 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 abnormal 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

Appendix I: Routine Assessment of Patient Index Data 3 (RAPID3) Score
The Routine Assessment of Patient Index Data 3 (RAPID3) is a pooled index of the three patient-reported ACR core data set measures: function, pain, and patient global estimate of status. Each of the individual measures is scored 0 – 10, and the maximum achievable score is 30.

RAPID3 Score	Disease state interpretation
≤ 3	Remission
3.1 to 6	Low disease activity
6.1 to 12	Moderate disease activity
> 12	High disease activity

Appendix J: Clinical Juvenile Arthritis Disease Activity Score based on 10 joints (cJADAS-10)
The cJADAS10 is a continuous disease activity score specific to JIA and consisting of the following three parameters totaling a maximum of 30 points:

- Physician's global assessment of disease activity measured on a 0-10 visual analog scale (VAS), where 0 = no activity and 10 = maximum activity;
- Parent global assessment of well-being measured on a 0-10 VAS, where 0 = very well and 10 = very poor;
- Count of joints with active disease to a maximum count of 10 active joints*

**ACR definition of active joint: presence of swelling (not due to currently inactive synovitis or to bony enlargement) or, if swelling is not present, limitation of motion accompanied by pain, tenderness, or both*

cJADAS-10	Disease state interpretation
≤ 1	Inactive disease
1.1 to 2.5	Low disease activity
2.51 to 8.5	Moderate disease activity
> 8.5	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 or 80 mg every other week.	40 mg/week

<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>PJIA</td><td>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</td><td>40 mg every other week</td></tr>
<tr><td>PsA
AS</td><td>40 mg SC every other week</td><td>40 mg every other week</td></tr>
<tr><td>CD</td><td><u>Initial dose:</u>
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

<u>Maintenance dose:</u>
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</td><td>40 mg every other week</td></tr>
<tr><td>UC</td><td><u>Initial dose:</u>
Adults: 160 mg SC on Day 1, then 80 mg SC on Day 15

Pediatrics:<table><tr><th>Weight</th><th>Days 1 through 15</th></tr><tr><td>20 kg to less than 40 kg</td><td>Day 1: 80 mg
Day 8: 40 mg
Day 15: 40 mg</td></tr><tr><td>40 kg and greater</td><td>Day 1: 160 mg (single dose or split over tw consecutive days
Day 8: 80 mg
Day 15: 80 mg</td></tr></table><u>Maintenance dose:</u>
Adults: 40 mg SC every other week starting on Day 29</td><td>40 mg every week</td></tr>
</table>

Indication	Dosing Regimen	Maximum Dose
	Pediatrics: **Weight** / **Starting on Day 29*** 20 kg to less than 40 kg: 40 mg every other week or 20 mg every week 40 kg and greater: 80 mg every other week or 40 mg every week **Continue the recommended pediatric dosage in patients who turn 18 years of age and who are well-controlled on Humira regimen.*	
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

Drug Name	Availability
	• Single-use vial for institutional use only: 40 mg/0.8 mL
Adalimumab-afzb (Abrilada)	• Single-dose prefilled pen (Abrilada Pen): 40 mg/0.8 mL • Single dose prefilled syringe: 40 mg/0.8 mL, 20 mg/0.4 mL, 10 mg/0.2 mL • Single-dose glass 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, 40 mg/0.4 mL (citrate-free) • Single-dose prefilled syringe: 40 mg/0.8 mL, 40 mg/0.4 mL (citrate-free) • Single-dose glass vial for institutional use only: 40 mg/0.8 mL
Adalimumab-fkjp (Hulio)	• Single-dose prefilled pen (Hulio Pen): 40 mg/0.8 mL • Single-dose prefilled syringe: 40 mg/0.8 mL, 20 mg/0.4 mL
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
Adalimumab-aacf (Idacio)	• Single-dose prefilled pen (Idacio Pen): 40 mg/0.8 mL • Single-dose prefilled glass syringe: 40 mg/0.8 mL

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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
J3590	Unclassified biologics

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created, adapted from CP.PHAR.242 Adalimumab (Humira), Humira Biosimilars for migration to HFS PDL.	1.13.2020	
2Q 2021 annual Review -Updated pJIA criteria to require diagnosis as evidenced by ≥ 5 joints, cJADAS assessment, Additionally, updated criteria to allow tiered redirection or bypass of MTX in the event of sacroiliitis or high disease activity. Added criteria for RAPID3 assessment for RA given limited in-person visits during COVID-19 pandemic, updated appendices; for UC, revised redirection from AZA, 6-MP, and ASA to corticosteroids	3.12.2021	
RT4: updated FDA approved indications to reflect pediatric extensions for Cyltezo in JIA and CD; updated criteria to reflect pediatric extension for UC to include patients 5 years of age and older; updated CDAI table with ">" to prevent overlap in classification of severity; clarified different therapeutic classes one must be tried for HS, for 3 months; added additional criteria related to diagnosis of moderate-to-severe PsO per 2019 AAD/NPF guidelines specifying at least 3% BSA involvement or involvement of areas that severely impact daily function; added combination of bDMARDs under Section III; references reviewed and updated.	11.24.21	
RT4: added biosimilars Abrilada and Hulio to policy; added new dosage form (single-dose glass vial) for Hadlima; updated FDA approved indications to reflect pediatric extensions for JIA and CD indications for Abrilada, Amjevita, Hadlima, Hulio, and Hyrimoz; added limitations of use for UC per PI	8.31.22	
RT4: added new dosage form (citrate-free 40 mg/0.4 mL PushTouch and prefilled syringe) for Hadlima. Template changes applied to other diagnoses/indications and continued therapy section; for AS added redirection to Xeljanz per SDC and updated FDA labeling; reiterated requirement against combination use with a bDMARD or JAKi from Section III to Sections I and II; for PsO, allowed phototherapy as alternative to systemic conventional DMARD if contraindicated or clinically significant adverse effects are experienced; references reviewed and updated	9.26.22	
Retire policy: t/f criteria removed	12.22.22	
Policy readapted to align with HFS PDL due to February SDC adaptation of Amjevita; Idacio biosimilar added; Humira listed as preferred agent in Section I	2.20.23	

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.

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.