Clinical Policy: Adalimumab (Humira)

Reference Number: AZ.CP.PHAR.25
Effective Date: 11.16.16
Last Review Date: 9.12.18
Line of Business: Medicaid - AHCS

Revision Log

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

Description

Adalimumab (Humira®) is a Tumor Necrosis Factor Inhibitor (TNFi).

FDA approved indication

Humira is indicated:

- **Rheumatoid Arthritis:** Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage and improving physical function in adult patients with moderately to severely active rheumatoid arthritis.
- **Psoriatic Arthritis:** Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active psoriatic arthritis.
- **Ankylosing spondylitis:** Reducing signs and symptoms in adult patients with active ankylosing spondylitis.
- **Adult Crohn`s Disease:** Reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn`s disease who have had an inadequate response to conventional therapy. Reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab.
- **Pediatric Crohn`s Disease:** Reducing signs and symptoms and inducing and maintaining clinical remission in patients 6 years of age and older with moderately to severely active Crohn's disease who have had an inadequate response to corticosteroids or immunomodulators such as azathioprine, 6-mercaptopurine, or methotrexate.
- **Ulcerative Colitis:** Inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine or 6-mercaptopurine (6-MP). The effectiveness of Humira has not been established in patients who have lost response to or were intolerant to TNF blockers.
- **Plaque Psoriasis:** Treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate.
- **Juvenile Idiopathic Arthritis:** Reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients 2 years of age and older.
- **Hidradenitis Suppurativa (HS):** Treatment of moderate to severe Hidradenitis Suppurativa.
- **Uveitis:** 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 health plans affiliated with Centene Corporation® that Humira is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Rheumatoid Arthritis (must meet all)**:**
1. Diagnosis of rheumatoid arthritis;
2. One of the following (a or b):
   a. Prescribed by or in consultation with a rheumatologist;
   b. Defined at baseline prior to disease modifying anti-rheumatic drug (DMARD) treatment initiation by the (American College of Rheumatology (ACR)) criteria (refer to General Information for ACR criteria);
3. One of the following (a or b):
   a. Failure of a trial of methotrexate (MTX) in the last year for patients who are new to biologics, unless contraindicated or clinically significant adverse effects are experienced;
   b. If patient is not a candidate for MTX (i.e., patient is a smoker (increased risk of MTX lung disease) or if MTX is otherwise contraindicated), then failure of a trial of sulfasalazine or one other DMARD;
4. Dose does not exceed 40 mg every other week. (If not on concomitant MTX, may benefit from increasing to 40 mg weekly).

Approval duration: 3 months

B. Psoriatic Arthritis (must meet all)**:**
1. Diagnosis of active psoriatic arthritis at baseline prior to initiation of DMARD therapy;
2. Confirmed by a rheumatologist or dermatologist
3. Member meets one of the following (a, b, or c) unless contraindicated or clinically significant adverse effects are experienced:
   a. Failure of ≥ 3 consecutive month trial of MTX up to maximally indicated doses
   b. If intolerance or contraindication to MTX, failure of a ≥ 3 consecutive month trial of cyclosporine, sulfasalazine, or leflunomide up to maximally indicated doses
   c. For axial disease, failure of a ≥ 4 week trial of NSAIDs up to maximally indicated doses
4. Dose does not exceed 40 mg every other week.

Approval duration: 3 months

C. Ankylosing spondylitis (must meet all)**:**
1. Diagnosis of moderate to severe ankylosing spondylitis;
2. Failure of a trial of at least two NSAIDs for at least 3 months at maximal recommended or tolerated anti-inflammatory dose, unless contraindicated or clinically significant adverse effects are experienced;
3. Dose does not exceed 40 mg every other week.

Approval Duration: 3 months

D. Crohn's Disease

1. Diagnosis of moderate to severe Crohn's Disease;
2. Confirmed by a gastroenterologist;
3. Failure of a ≥ 3 consecutive month trial of at least ONE immunomodulator (e.g., azathioprine, 6-mercaptopurine [6-MP], MTX) up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced
4. Maintenance dose does not exceed 40 mg every other week.

Approval Duration: 3 months

E. Ulcerative Colitis

1. Diagnosis of moderate to severe ulcerative colitis;
2. Confirmed by a gastroenterologist;
3. For Induction, both of the following (a and b):
   a. Patient is not in remission;
   b. Failure to a one-month course of aminosalicylates (e.g., sulfasalazine, mesalamine) followed by corticosteroids such as prednisone, unless contraindicated or clinically significant adverse effects are experienced;
4. For Maintenance: Failure of a trial of one of the following unless contraindicated or clinically significant adverse effects are experienced:
   a. Azathioprine;
   b. 6-mercaptopurine (6-MP);
   c. Aminosalicylates (sulfasalazine, mesalamine);
5. Dose does not exceed:
   a. Induction: 160 mg day 1 (or split over 2 days), followed by 80 mg two weeks later, then begin maintenance dose;
   b. Maintenance: 40 mg every other week.

Approval Duration: 3 months

F. Plaque Psoriasis

1. Diagnosis of moderate to severe plaque psoriasis;
2. Confirmed by a dermatologist or rheumatologist;
3. One of the following:
   a. Psoriasis affects 5% or more of the body;
   b. Psoriasis involves hands, feet, head and neck or genitalia;
   c. Failure or clinically significant adverse effects to topical therapy (e.g., calcipotriene, Tazorac®, topical steroids;
4. Failure of a trial of ONE of the following therapies, either alone or in combination, unless contraindicated or clinically significant adverse effects are experienced:
   a. MTX up to a dose of 15-20 mg/week;
   b. If MTX is contraindicated, failure or clinically significant adverse effects to PUVA / UVB therapy or cyclosporine;
5. Dose does not exceed 80 mg (one time initial dose), followed by 40 mg every other week starting one week after the initial dose.

Approval Duration: 3 months

G. Polyarticular Juvenile Idiopathic Arthritis

1. Diagnosis of polyarticular juvenile idiopathic arthritis;
2. Confirmed by a rheumatologist;
3. Failure of a 3 month trial of MTX, unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed:
   a. Weight 10 to < 15 kg: 10 mg every other week;
   b. Weight 15 to < 30 kg: 20 mg every other week;
   c. Weight ≥ 30 kg: 40 mg every other week.

Approval Duration: 3 months

H. Hydradenitis Suppurativa (HS)

1. Diagnosis of HS;
2. Prescribed by a dermatologist, rheumatologist or gastroenterologist;
3. Dose does not exceed 160 mg day 1 (or split over 2 days), followed by 80 mg two weeks later, then begin maintenance dose, then 40 mg weekly.

Approval Duration: 3 months

I. Uveitis

1. Diagnosis of uveitis;
2. Prescribed by an ophthalmologist;
3. Dose does not exceed 80 mg (one time initial dose), followed by 40 mg every other week starting one week after the initial dose.

Approval Duration: 3 months

J. Other Diagnoses / Indications:

1. Refer to 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 a health plan affiliated with Centene Corporation or member has previously met initial approval criteria;
2. Documentation of positive response to therapy;
3. If request is for a dose increase, new dose does not exceed those listed in Section I for the relevant indication.

Approval duration: Up to one year

B. 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 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 the off-label use policy – CP.PHAR.57 or evidence of coverage documents;

B. Combination use with Xeljanz or biological DMARDs such as TNF antagonists [Cimzia, Enbrel, Simponi, Remicade], interleukin-1 receptor (IL-1R) antagonists [Kineret], interleukin-6 receptor (IL-6R) antagonists [Actemra], anti-CD20 monoclonal antibodies [Rituxan] and selective co-stimulation modulators [Orencia] because of the possibility of increased immunosuppression, neutropenia and increased risk of infection.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DMARD: disease-modifying anti-rheumatic drug

Appendix B: General Information

- ACR Classification criteria for RA (score-based algorithm: add score of categories A-D; a score of >/= 6/10 is needed for classification of a patient as having definite RA).
  A. Joint involvement (swollen or tender)
     - 1 large joint, score = 0
     - 2-10 large joints, score = 1
     - 1-3 small joints (with or without involvement of large joints), score = 2
     - 4-10 small joints (with or without involvement of large joints), score = 3
     - >10 joints (at least 1 small joint), score = 5

  B. Serology (at least 1 test result is needed for classification)
     - Negative RF (rheumatoid factor) and negative ACPA (anti-citrullinated protein antibody), score = 0
     - Low-positive RF or low-positive ACPA, score = 2
     - High-positive RF or high-positive ACPA, score = 3

  C. Acute-phase reactants (at least 1 test result is needed for classification)
     - Normal CRP (C-reactive protein) and normal ESR (erythrocyte sedimentation rate), score = 0
     - Abnormal CRP or abnormal ESR, score = 1

  D. Duration of symptoms
     - < 6 weeks, score = 0
     - >/= 6 weeks, score = 1
- In RA, failure of MTX or DMARD is defined as a contraindication or ≤ 50% decrease in swollen joint count, ≤ 50% decrease in tender joint count, and ≤ 50% decrease in ESR, or ≤ 50% decrease in CRP, or contraindication to at least 3 months of therapy with MTX at doses up to 25 mg per week or maximum tolerated dose.
- This agent is immunosuppressive and has the potential to increase the risk of infection and reactivate latent, chronic infections. It should not be administered to patients with a clinically important infection. Caution should be used in patients with chronic infections or history of recurrent infection. If patient develops a serious infection this agent should be discontinued.

- Two clinical trials of two years duration failed to demonstrate that TNF inhibition reduced radiographic progression of structural damage.
- Several ankylosing spondylitis (AS) treatment guidelines call for a trial of 2 or 3 non-steroidal anti-inflammatory drugs (NSAID) prior to use of an anti-TNF agent. A two year trial showed that continuous NSAID use reduced radiographic progression of AS versus on demand use of NSAID.
- Serious infections were seen in clinical studies with concurrent use of Kineret and another TNF-blocking agent, Enbrel, with no added benefit compared to Enbrel alone. Because of the nature of the adverse reactions with this combination therapy, similar toxicities may also result from combination of anakinra and other tumor necrosis factor (TNF) blocking agents.
- For Ulcerative Colitis maintenance therapy, failure is defined as having two or more exacerbations requiring steroid therapy.
- Failure of MTX in PJIA is defined as disease activity remaining moderate to high despite treatment with MTX.
- In PJIA, response to treatment is reflected by improvement of disease activity level and poor prognostic features including: reduction in the number of active joints, ESR or CRP, Physician global assessment, patient/parent global assessment, arthritis of the hip or cervical spine, positive RF or ACPA, radiographic damage.
- Per prescribing information, Xeljanz should not be used in combination with biologic DMARDs [such as Kineret] or potent immunosuppressants such as azathioprine and cyclosporine. As stated in the black box warning, patients treated with Xeljanz are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as MTX or corticosteroids.
- Hidradenitis Suppurativa (HS) 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. "

Appendix C: Therapeutic Alternatives

Drug	Dosing Regimen	Dose/Limit/Maximum Dose
Imuran (azathioprine)	**Rheumatoid Arthritis** 1 mg/kg/day PO given as a single dose or in divided doses twice daily **Crohn's Disease and Ulcerative Colitis** 100 - 250 mg PO daily	2.5 mg/kg/day
Dovonex® (calcipotriene)	**Plaque Psoriasis** Apply topically BID	N/A
Cimzia® (certolizumab pegol)**	**Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis** 400 mg SC initially and at Weeks 2 and 4. Maintenance dose: 200 mg SC every other week or 400 mg SC every 4 weeks	Initial: 1200 mg Maintenance: 400 mg/month

Drug	Dosing Regimen	Dose/Limit/Maximum Dose
	Crohn's Disease Initial dose: 400 mg SC initially and at weeks 2 and 4. Maintenance dose: 400 mg SC every 4 weeks.	
Corticosteroids	**Crohn's Disease** Prednisone 40 mg PO daily for 2 weeks or IV 50-100 mg Q6H for 1 week budesonide (Entocort EC®)6-9 mg PO daily	Varies
Gengraf, Neoral (Cyclosporine)	**Rheumatoid Arthritis, Plaque Psoriasis** 2.5 – 4 mg/kg/day PO divided BID	4 mg/kg/day
Enbrel® (etanercept)*	**Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis** 25 mg SC twice weekly or 50 mg SC once weekly **Plaque Psoriasis** 25-50 mg SC twice weekly or 50 mg SC once weekly **Polyarticular Juvenile Idiopathic Arthritis** Less than 63 kg: 0.8 mg/kg SC per week given as single injection. 63 kg or more: 50 mg SC per week	**Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Polyarticular Juvenile Idiopathic Arthritis** 50 mg per week
Plaquenil® (hydroxychloroquine)	**Rheumatoid Arthritis** Initial dose: 400-600 mg PO daily Maintenance dose: 200-400 mg PO daily	600 mg/day
mercaptopurine	**Crohn's Disease, Ulcerative Colitis** 75 – 125 mg PO daily	1.5 mg/kg/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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Rheumatoid Arthritis	40 mg SC QOW If not on concomitant methotrexate, may benefit from increase to 40mg weekly	40 mg weekly Escalation to this dose will require documentation of partial response to

		QOW dosing
Ankylosing Spondylitis	40 mg SC QOW	40 mg QOW
Adult Crohn's Disease	Induction: 160 mg SC day 1 (or split over 2 days) followed by 80 mg 2 weeks later, then begin maintenance 2 weeks following 80 mg dose Maintenance: 40 mg SC QOW	Maintenance: 40 mg SC QOW
Pediatric Crohn's Disease	17 to < 40 kg: 80 mg day 1 followed by 40 mg 2 weeks later, then begin maintenance 2 weeks following 40 mg dose Maintenance: 20 mg SC QOW ≥ 40 kg: Same as adult dosing above	Maintenance: 20mg QOW Maintenance: 40 mg QOW
Ulcerative Colitis	Induction: 160 mg SC day 1 (or split over 2 days) followed by 80 mg 2 weeks later, then begin maintenance 2 weeks following 80 mg dose Maintenance: 40 mg SC QOW	Maintenance: 40 mg QOW
Plaque Psoriasis	Initial dose of 80 mg SC followed by 40mg SC QOW starting one week after initial dose	40mg QOW
Polyarticular Juvenile Idiopathic Arthritis	10 to <15 kg: 10 mg SC QOW 15 to <30 kg: 20 mg SC QOW ≥ 30 kg: 40 mg SC QOW	40 mg QOW
Hidradenitis Suppurativa	Initially 160 mg SC day 1 (or split over 2 days) followed by 80 mg 2 weeks later, then begin maintenance 2 weeks following 80 mg dose. Maintenance: 40 mg SC QW	40 mg weekly
Uveitis	Initial dose of 80 mg SC followed by 40mg SC QOW starting one week after initial dose	40 mg QOW

VI. Product Availability

- Pre-filled Pen Carton: 2 dose trays. Each dose tray contains a single-use 40 mg/0.8 ml pen.
- Crohn`s Disease/Ulcerative Colitis Starter Package: 6 dose trays. Each dose tray contains a single-use 40 mg/0.8 ml prefilled pen.
- Psoriasis Starter Package: 4 dose trays. Each dose tray contains a single-use 40 mg/0.8 ml prefilled pen.

- Pre-filled Syringe Carton: 40 mg: 2 dose trays. Each dose tray contains a single-use 40 mg/0.8 ml prefilled syringe.
- Pre-filled Syringe Carton: 20 mg: 2 dose trays. Each dose tray contains a single-use 20 mg/0.4 ml prefilled syringe.
- Pre-filled Syringe Carton: 10 mg: 2 dose trays. Each dose tray contains a single-use 10 mg/0.2 ml prefilled syringe.
- Pediatric Crohn`s Disease Starter Package: 3 dose trays or 6 dose trays. Each dose tray contains a single-use 40 mg/0.8 ml prefilled syringe.

VII. References

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template; minor changes to verbiage and grammar. References updated.	6/20/17	11.17
Updated criteria for both psoriatic arthritis and Crohn's Disease- specified verbiage to trial 3 months of MTX	9/12/18	

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.

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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.