Humira

Description

Humira (adalimumab)

Background
Humira is grouped within a class of medications called biologic response modifiers ("biologics") also called tumor necrosis factor (TNF) blockers. By working on the immune system, biologics block proteins that contribute to the disease process. TNF blockers suppress the immune system by blocking the activity of TNF, a substance in the body that can cause inflammation and lead to immune-system diseases, such as Crohn’s disease, ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and plaque psoriasis. The drugs in this class include Remicade (infliximab), Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab pegol) and Simponi (golimumab) (1). Humira reduces levels of the active form of TNF. Humira may be used alone or in combination with non-biologic disease-modifying antirheumatic drugs (DMARDs) (2).

Regulatory Status
FDA-approved indication: Humira is a tumor necrosis factor (TNF) blocker indicated for the treatment of: (2)

Rheumatoid Arthritis (RA) - Humira is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis (RA). Humira can be used alone or in combination with methotrexate (MTX) or other non-biologic disease-modifying anti-rheumatic drugs (DMARDs).
Polyarticular Juvenile Idiopathic Arthritis (pJIA) - Humira is indicated for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA) in patients aged 2 years or older. Humira can be used alone or in combination with methotrexate (MTX).

Psoriatic Arthritis (PsA) - Humira is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active psoriatic arthritis (PsA). Humira can be used alone or in combination with non-biologic DMARDs.

Ankylosing Spondylitis (AS) - Humira is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis (AS).

Crohn’s Disease (CD) - Humira is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult patients and pediatric patients (6 years of age and older) with moderately to severely active Crohn’s disease who have had an inadequate response to conventional therapy. Humira is indicated for reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab.

Ulcerative Colitis (UC) - Humira is indicated for 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 (PsO) - Humira is indicated for the treatment of adult patients with chronic moderate to severe plaque psoriasis (PsO) who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate. Humira should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician.

Hidradenitis Suppurativa (HS) - The treatment of moderate to severe hidradenitis suppurativa.

Humira carries boxed warnings regarding serious infections and malignancies. Because Humira suppresses the immune system, patients are at a greater risk for getting serious infections leading to hospitalization or death, including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens. Lymphoma and other malignancies have been reported in children and adolescent patients.
Hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including Humira (2). Patients should be screened for latent tuberculosis infection. Patients at risk for hepatitis B virus (HBV) infection should be evaluated for evidence of prior HBV infection. Hepatitis B virus carriers should be monitored for reactivation during and several months after therapy. Humira should not be used in combination with other biologic agents. Humira should not be initiated in patients with an active infection. Humira should be discontinued if a patient develops a serious infection or sepsis during treatment (2).

Pancytopenia, aplastic anemia, cytopenia, lupus-like syndrome, anaphylaxis reactions, and congestive heart failure (new onset or worsening) may develop during Humira therapy and therapy should be discontinued (2).

Use of Humira with anakinra, abatacept, or cyclophosphamide is not recommended as the use may increase the risk of serious adverse events, including infections (2).

**Off-label use:**
There is sufficient medical literature to support the use of Humira in adolescent for the treatment of rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, plaque psoriasis, ulcerative colitis and plaque psoriasis (3-21).

The use of Humira for pediatric UC (ulcerative colitis) is not uncommon and comes from several sensible conclusions about similar medications that are FDA-approved for pediatric patients with inflammatory bowel disease (IBD) (3-21).

Humira has successfully treated refractory uveitis in children, adolescents and adults. In a retrospective study, 60 adult patients with uveitis were treated over an average follow-up period of 88 weeks. 49 out of 60 (81.7%) patients improved, while the other 11 (18.3%) patients did not meet improvement criteria and were given additional or alternative immunosuppressive treatment. At the last follow-up, 47 (78.3%) patients were still on Humira treatment. The results proved effective for 80% of patients with uveitis. It is also noted that Humira can be used in children and adolescents with uveitis (22-23).

**Related policies**
Actemra, Cimzia, Cosentyx, Enbrel, Kineret, Orencia, Remicade, Rituxan, Simponi, Stelara, Xeljanz
Humira may be considered medically necessary in patients 2 years of age and older with moderately to severely active Polyarticular Juvenile Idiopathic Arthritis (JIA); in patients 6 years and older with Crohn’s Disease (CD), in patients 12 years of age and older with moderately to severely active Rheumatoid Arthritis (RA), Active Psoriatic Arthritis (PsA), Active Ankylosing Spondylitis (AS), Ulcerative Colitis (UC), or Chronic moderate to severe Plaque Psoriasis (PsO) who have inadequate response, intolerance, or contraindication to systemic therapy or phototherapy, also for patients with uveitis and Hidradenitis Suppurativa (HS); with a negative test for latent TB infection or is receiving treatment or has completed treatment for latent TB, not at risk for HBV infection or HBV infection has been ruled out or treatment for HBV has been initiated, absent of active infection, and not taken in combination with another biologic agent.

Humira is considered investigational in patients that do not meet the above criteria.

Prior-Approval Requirements

Diagnoses

Patient must have ONE of the following:

**Age** 2 years of age or older

1. Moderately to severely active Polyarticular Juvenile Idiopathic Arthritis (JIA)

**Age** 6 years of age or older

1. Crohn’s Disease (CD)

**Age** 12 years of age or older

1. Moderately to severely active Rheumatoid Arthritis (RA)
2. Active Psoriatic Arthritis (PsA)
3. Active Ankylosing Spondylitis (AS)
4. Ulcerative Colitis (UC)
5. Chronic moderate to severe Plaque Psoriasis (PsO)
   a. Inadequate response, intolerance, or contraindication to either conventional systemic therapy or phototherapy

6. Uveitis

7. Hidradenitis Suppurativa (HS)

AND ALL of the following:
1. Result for latent TB infection is negative OR result was positive for latent TB and patient completed treatment (or is receiving treatment) for latent TB
2. Patient is not at risk for HBV infection OR patient is at risk for HBV infection and HBV infection has been ruled out or treatment for HBV infection has been initiated.
3. Absence of active infection (including tuberculosis and hepatitis B virus (HBV)
4. Not used in combination with another biologic agent

Prior – Approval Renewal Requirements

Diagnoses

Patient must have ONE of the following:

**Age 2 years of age or older**

1. Polyarticular Juvenile Idiopathic Arthritis (JIA)

**Age 6 years of age or older**

1. Crohn’s Disease (CD)

**Age 12 years of age or older**

1. Rheumatoid Arthritis (RA)
2. Psoriatic Arthritis (PsA)
3. Ankylosing Spondylitis (AS)
4. Ulcerative Colitis (UC)
5. Chronic moderate to severe Plaque Psoriasis (PsO)
6. Uveitis
7. Hidradenitis Suppurativa (HS)
AND ALL of the following:
1. Condition has improved or stabilized with Humira
2. Absence of active infection (including tuberculosis and hepatitis B virus (HBV))
3. Not used in combination with another biologic agent

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits
Duration 12 months

Prior – Approval Renewal Limits
Duration 18 months

Rationale

Summary
Humira is a tumor necrosis factor (TNF) blocker indicated for the treatment of polyarticular juvenile idiopathic arthritis (JIA), moderately to severely active rheumatoid arthritis (RA), active psoriatic arthritis (PsA), active ankylosing spondylitis (AS), Crohn’s disease (CD), ulcerative colitis (UC), or chronic moderate to severe plaque psoriasis (PsO) who are candidates for systemic therapy or phototherapy. Humira has also used for the treatment of patients with uveitis and Hidradenitis Suppurativa (HS). These patients must have a negative test for latent TB infection or is receiving treatment or has completed treatment for latent TB, not at risk for HBV infection or HBV infection has been ruled out or treatment for HBV has been initiated, absent of active infection, and not taken in combination with another biologic agent.

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Humira while maintaining optimal therapeutic outcomes.

References
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19. Afif W et al. Open-label study of adalimumab in patients with ulcerative colitis including those with prior loss of response to infliximab. Inflam Bowel Dis 2009;Apr 30:[Epub ahead of publication].


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<td>Addition to PA</td>
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<tr>
<td>September 2014</td>
<td>Age limit lowered to 12 and older for RA, PsA, AS, UC, PsO and renewal limit to 18 months, age limit lowered to 6 and older for CD. Annual editorial review and reference update</td>
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<tr>
<td>October 2014</td>
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<td>Addition of off-Label indications: uveitis and hidradenitis suppurativa (HS)</td>
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Keywords
This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 3, 2015 and is effective January 1, 2016.

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