**RATIONALE FOR INCLUSION IN PA PROGRAM**

**Background**

Humira and its biosimilars are 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 and Amjevita reduce levels of the active form of TNF. Humira and its biosimilars may be used alone or in combination with non-biologic disease-modifying antirheumatic drugs (DMARDs) (2-8).

**Regulatory Status**

FDA-approved indication: Humira and its biosimilars are tumor necrosis factor (TNF) blockers indicated for the treatment of: (2-8)

**Rheumatoid Arthritis (RA)** – Humira and its biosimilars are 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 and its biosimilars are indicated for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA). Humira is indicated in patients aged 2 years or older and Amjevita is indicated in patients aged 4 years and older. Humira and Amjevita can be used alone or in combination with methotrexate (MTX).
Psoriatic Arthritis (PsA) – Humira and its biosimilars are 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 and Amjevita can be used alone or in combination with non-biologic DMARDs.

Ankylosing Spondylitis (AS) – Humira and its biosimilars are indicated for reducing signs and symptoms in patients with active ankylosing spondylitis (AS).

Crohn’s Disease (CD) – Humira and its biosimilars are indicated for 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. Additionally, Humira and its biosimilars are indicated for reducing signs and symptoms and inducing clinical remission in 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 and its biosimilars are 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 and its biosimilars are 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 and its biosimilars have not been established in patients who have lost response to or were intolerant to TNF blockers.

Plaque Psoriasis (Ps) – Humira and its biosimilars are indicated for the treatment of adult patients with chronic moderate to severe plaque psoriasis (Ps) who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate. Humira and its biosimilars should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician.
HUMIRA (adalimumab), ABRILADA* (adalimumab-afzb), AMJEVITA* (adalimumab-atto), CYLTEZO* (adalimumab-adbm), HADLIMA* (adalimumab-bwwd), HULIO* (adalimumab-fkj), HYRIMOZ* (adalimumab-adaz)

*These medications are included in this policy but are not available in the market as of yet

FDA-approved indications for Humira only:

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

Uveitis (UV) - The treatment of non-infectious intermediate, posterior and panuveitis in adults and pediatric patients 2 years of age and older.

Humira and its biosimilars carry boxed warnings regarding serious infections and malignancies. Because Humira and its biosimilars suppress 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 treated with TNF blockers. Hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including Humira (2-8).

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 and its biosimilars should not be used in combination with other biologic agents. Humira should not be initiated in patients with an active infection. Humira and its biosimilars should be discontinued if a patient develops a serious infection or sepsis during treatment (2-8).

Pancytopenia, aplastic anemia, cytopenia, lupus-like syndrome, anaphylaxis reactions, and congestive heart failure (new onset or worsening) may develop during Humira or its biosimilars therapy and therapy should be discontinued (2-8).

Use of Humira or its biosimilars with anakinra, abatacept, or cyclophosphamide is not recommended as the use may increase the risk of serious adverse events, including infections (2-8).
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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 (9-23).

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) (9-23).

The FDA defines biosimilar as a biological product that is highly similar to and has no clinically meaningful
differences from an existing FDA-approved reference product. A manufacturer developing a proposed
biosimilar demonstrates that its product is highly similar to the reference product by extensively analyzing
the structure and function of both the reference product and the proposed biosimilar. Minor differences
between the reference product and the proposed biosimilar in clinically inactive components are
acceptable. Manufacturers must also demonstrate that its proposed biosimilar has no clinically meaningful
differences from the reference product in terms of safety, purity, and potency (safety and effectiveness)
(24).

Summary
Humira and its biosimilars are tumor necrosis factor (TNF) blockers 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 is also indicated 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
HUMIRA (adalimumab), ABRILADA* (adalimumab-afzb), AMJEVITA* (adalimumab-atto),
CYLTEZO* (adalimumab-adbm), HADLIMA* (adalimumab-bwwd), HULIO* (adalimumab-fkjp),
HYRIMOZ* (adalimumab-adaz)

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with another biologic agent (1-23).

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

References
HUMIRA (adalimumab), ABRILADA* (adalimumab-afzb), AMJEVITA* (adalimumab-atto),
CYLTEZO* (adalimumab-adbm), HADLIMA* (adalimumab-bwwd), HULIO* (adalimumab-fkjp),
HYRIMOZ* (adalimumab-adaz)

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21. 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].