RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Humira and Amjevita 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 Amjevia may be used alone or in combination with non-biologic disease-modifying antirheumatic drugs (DMARDs) (2-3).

Regulatory Status
FDA-approved indication: Humira and Amjevita are tumor necrosis factor (TNF) blockers indicated for the treatment of: (2-3)

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

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

**Crohn’s Disease (CD)** – Humira and Amjevita 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 is 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 Amjevita 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 Amjevita 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 Amjevita have not been established in patients who have lost response to or were intolerant to TNF blockers.

**Plaque Psoriasis (Ps)** – Humira and Amjevita 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 Amjevita should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician.

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 Amjevita carry boxed warnings regarding serious infections and malignancies. Because Humira and Amjevita 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 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 (2-3).

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 Amjevita should not be used in combination with other biologic agents. Humira should not be initiated in patients with an active infection. Humira and Amjevita should be discontinued if a patient develops a serious infection or sepsis during treatment (2-3).

Pancytopenia, aplastic anemia, cytopenia, lupus-like syndrome, anaphylaxis reactions, and congestive heart failure (new onset or worsening) may develop during Humira or Amjevita therapy and therapy should be discontinued (2-3).

Use of Humira or Amjevita with anakinra, abatacept, or cyclophosphamide is not recommended as the use may increase the risk of serious adverse events, including infections (2-3).

**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 (4-18).

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) (4-18).
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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) (19).

Summary
Humira and Amjevita 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 with another biologic agent (1-18).

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

References
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