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Federal Employee Program.

HUMIRA (adalimumab), **ABRILADA*** (adalimumab-afzb),

AMJEVITA* (adalimumab-atto), **CYLTEZO*** (adalimumab-adbm),

HADLIMA* (adalimumab-bwwd), **HULIO*** (adalimumab-fkjp), **HYRIMOZ*** (adalimumab-adaz)

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

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 indications: 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 adult 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).



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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 adult patients with active ankylosing spondylitis (AS).

Crohn's Disease (CD) – Humira and its biosimilars are indicated for the treatment of moderately to severely active Crohn's disease in adults and pediatric patients 6 years of age and older.

Ulcerative Colitis (UC) - Humira and its biosimilars are indicated for with the treatment of moderately to severely active ulcerative colitis in adults and pediatric patients 5 years of age and older. Limitations of Use: 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 (PsO) – Humira and its biosimilars are indicated for the treatment of adult patients with chronic moderate to severe chronic plaque psoriasis (PsO) 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.

FDA-approved indications for Humira only (2):

Hidradenitis Suppurativa (HS) - The treatment of moderate to severe hidradenitis suppurativa in patients 12 years of age and older.

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



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Humira and its biosimilars carry boxed warnings regarding serious infections and malignancies. Because Humira and its biosimilars 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 (2-8).

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).

Off-label uses:

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).



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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 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



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1. US Food and Drug Administration Website. Drug Safety. Accessed February 2021.
<http://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm109340.htm>
2. Humira [package insert]. North Chicago, IL: AbbVie Inc.; February 2021.
3. Amjevita [package insert]. Thousand Oaks, CA: Amgen Inc.; September 2016.
4. Cyltezo [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; August 2017.
5. Hyrimoz [package insert]. Princeton, NJ: Sandoz Inc.; October 2018.
6. Hadlima [package insert]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp.; July 2019.
7. Abrilada [package insert]. New York, NY: Pfizer Inc.; November 2019.
8. Hulio [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; July 2020.
9. Gartlehner G et al. Biologics for the treatment of juvenile idiopathic arthritis: a systematic review and critical analysis of the evidence. *Clin Rheumatol* 2008;27:67-76.
10. Sulpice M et al. Efficacy and safety of anti-TNF alpha therapy in patients with juvenile spondyloarthritis. *Joint Bone Spine* 2009;76:24.
11. Sieper J et al. Adalimumab for treatment of ankylosing spondylitis . *Expert Opin Pharmacother* 2007;8:831.
12. Tse SM et al. Anti-TNF alpha blockade in treatment of juvenile spondyloarthritis. *Arthritis Rheum* 2005;52:2103.
13. Gartlehner G et al. Biologics for the treatment of juvenile idiopathic arthritis: a systematic review and critical analysis of the evidence. *Clin Rheumatol* 2008;27:67-76.
14. Saeed SA, Crandall WV. Managing Crohn's disease in children and adolescents: focus on TNF antagonists. *Paediatr Drugs* 2008;10:31-38.
15. Noe JD, Pfeffakorn M. Short-term response to Adalimumab in childhood inflammatory bowel disease. *Inflam Bowel Dis* 2008;14:1683-87.
16. Rosh JR, Lerer T, Markowitz J, Goli SR, Mamula P, Noe JD, Pfefferkorn MD, Kelleher KT, Griffiths AM, Kugathasan S, Keljo D, Oliva-Hemker M, Crandall W, Carvalho RS, Mack DR, Hyams JS. Retrospective Evaluation of the Safety and Effect of Adalimumab Therapy (RESEAT) in pediatric Crohn's disease. *Am J Gastroenterol*. 2009 Dec;104(12):3042-9.



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17. Viola F, Civitelli F, Di Nardo G, Barbato MB, Borrelli O, Oliva S, Conte F, Cucchiara S. Efficacy of adalimumab in moderate-to-severe pediatric Crohn's disease. *Am J Gastroenterol*. 2009 Oct;104(10):2566-71.
18. Evers EA et al. Factors predictive of Crohn disease following colectomy in medically refractory pediatric colitis. *J Pediatr Gastroenterol Nutr* 2009;48:283-286.
19. Trinder MW, Lawrance IC. Efficacy of adalimumab for the management of inflammatory bowel disease in the clinical setting. *J Gastroenterol Hepatol* 2009;Feb 11:[Epub ahead of publication].
20. Swaminath A et al. Early clinical experience with adalimumab treatment of inflammatory bowel disease with infliximab-treated and naïve patients. *Aliment Pharmacol Ther* 2009;29:273-278.
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].
22. Smita V. Sukhatme, Alice B. Gottlieb. Pediatric psoriasis: updates in biologic therapies. *Dermatologic Therapy*. Volume 22, Issue 1, pages 34–39, January/February 2009.
23. *Dermatology*. Jean Bolognia, et al. 3rd edition. Philadelphia, PA: Saunders, Inc.; 2012.
24. Biosimilar and Interchangeable Products. U.S. Food & Drug Administration. October 23, 2017. Accessed February 2021.
<https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm580419.htm#generic>