BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
1310 G Street, N.W.
Washington, D.C. 20005
202.942.1000
Fax 202.942.1125

5.70.029

Section:	Prescription Drugs	**Effective Date:**	January 1, 2024
Subsection:	Analgesics and Anesthetics	**Original Policy Date:**	November 11, 2013
Subject:	Humira	**Page:**	1 of 21

Last Review Date: December 8, 2023

Humira

Description

Humira (adalimumab)
Abrilada** (adalimumab-afzb)
Amjevita (adalimumab-atto)
Cyltezo* (adalimumab-adbm)
Hadlima* (adalimumab-bwwd)
Hulio* (**adalimumab-fkjp**)
Hyrimoz (adalimumab-adaz)
Idacio* (adalimumab-aacf)
Yuflyma* (adalimumab-aaty)
Yusimry* (adalimumab-aqvh)

Preferred products: Humira, adalimumab-fkjp, Hyrimoz, adalimumab-adaz
*Prior authorization for specific formulations applies only to formulary exceptions due to being a non-covered medication.

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

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) (2-11).

Regulatory Status
FDA-approved indications: Humira and its biosimilars are tumor necrosis factor (TNF) blockers indicated for the treatment of: (2-11)

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).

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.

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 (2-11).

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 (2-11).

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 (2-11).

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 (2-11).

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 (12-26).

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) (12-26).

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) (27).

Related policies
Cimzia, Enbrel, Infliximab, Simponi

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Humira and its biosimilars may be considered **medically necessary** if the conditions indicated below are met.

Humira and its biosimilars may be considered **investigational** for all other indications.

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 (pJIA)

a. Inadequate treatment response, intolerance, or contraindication to a 3-month trial of at least **ONE** conventional disease-modifying antirheumatic drugs (DMARDs) (see Appendix 1)
b. Prescriber will be dosing the patient within the FDA labeled maintenance dose of the following:
    i. Age 2-17, weight 10kg to < 15kg: 10 mg every other week
    ii. Age 2-17, weight 15kg to < 30kg: 20 mg every other week
    iii. Age 2-17, weight ≥30kg: 40 mg every other week
    iv. Age 18 and older: 40 mg every other week

2. Uveitis
    a. Prescriber will be dosing the patient within the FDA labeled maintenance dose of the following:
        i. Age 2-17, weight 10kg to < 15kg: 10 mg every other week
        ii. Age 2-17, weight 15kg to < 30kg: 20 mg every other week
        iii. Age 2-17, weight ≥30kg: 40 mg every other week
        iv. Age 18 and older: 40 mg every other week

Age 5 years of age or older

1. Ulcerative Colitis (UC)
    a. Inadequate treatment response, intolerance, or contraindication to at least **ONE** conventional therapy option (see Appendix 2)
    b. Prescriber will be dosing the patient within the FDA labeled maintenance dose of the following:
        i. Age 5-17, weight 20kg to <40kg: 40 mg every other week or 20 mg every week
        ii. Age 5-17, weight ≥40kg: 80 mg every other week or 40 mg every week
        i. Age 18 and older: 40 mg every other week **OR** 20 mg every week, or 40 mg every week/80 mg every other week if patient was established and stable on pediatric dosing regimen

Age 6 years of age or older

1. Moderate to severely active Crohn's Disease (CD)
    a. Inadequate treatment response, intolerance, or contraindication to at least **ONE** conventional therapy option (see Appendix 2)
    b. Prescriber will be dosing the patient within the FDA labeled maintenance dose of the following:
        i. Age 6-17, weight 17kg to < 40kg: 20 mg every other week
        ii. Age 6-17, weight ≥40kg: 40 mg every other week
        iii. Age 18 and older: 40 mg every other week

Age 12 years of age or older

1. Moderately to severely active Rheumatoid Arthritis (RA)
    a. Inadequate treatment response, intolerance, or contraindication to a 3-month trial of at least **ONE** conventional disease-modifying antirheumatic drugs (DMARDs) (see Appendix 1)
    b. Prescriber will be dosing the patient within the FDA labeled maintenance dose of the following:
        i. Concurrent therapy with methotrexate: 40 mg every other week
        ii. **NO** concurrent therapy with methotrexate: 40 mg every week or 80 mg every other week

2. Active Psoriatic Arthritis (PsA)
    a. Inadequate treatment response, intolerance, or contraindication to a 3-month trial of at least **ONE** conventional DMARD (see Appendix 1)
    b. Prescriber will be dosing the patient within the FDA labeled maintenance dose of 40 mg every other week

3. Active Ankylosing Spondylitis (AS)

a. Inadequate treatment response, intolerance, or contraindication to at least **TWO** non-steroidal anti-inflammatory drugs (NSAIDs)
b. Prescriber will be dosing the patient within the FDA labeled maintenance dose of 40 mg every other week

4. Chronic moderate to severe Plaque Psoriasis (PsO)
    a. Inadequate treatment response, intolerance, or contraindication to either conventional systemic therapy (see Appendix 1) or phototherapy
        i. If the patient is intolerant or contraindicated to one therapy then the patient must have an inadequate treatment response, intolerance, or contraindication to the other treatment option
    b. Prescriber will be dosing the patient within the FDA labeled maintenance dose of 40 mg every other week

5. Hidradenitis Suppurativa (HS)
    a. Prescriber will be dosing the patient within the FDA labeled maintenance dose of the following:
        i. Age 12-17, weight 30 kg to <60kg: 40 mg every other week
        ii. Age 12-17, weight ≥60kg: 40 mg every week or 80 mg every other week
        iii. Age 18 and older: 40 mg every week or 80 mg every other week

AND ALL of the following:

a. 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
b. 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
c. Absence of active infection [including tuberculosis and hepatitis B virus (HBV)]
d. **NOT** to be used in combination with any other biologic DMARD or targeted synthetic DMARD (see Appendix 1)
e. **NOT** given concurrently with live vaccines

Prior – Approval *Renewal* Requirements

Diagnoses

Patient must have **ONE** of the following:

Age 2 years of age or older

1. Polyarticular Juvenile Idiopathic Arthritis (pJIA)
   a. Prescriber will be dosing the patient within the FDA labeled maintenance dose of the following:
      i. Age 2-17, weight 10kg to < 15kg: 10 mg every other week
      ii. Age 2-17, weight 15kg to < 30kg: 20 mg every other week
      iii. Age 2-17, weight ≥30kg: 40 mg every other week
      iv. Age 18 and older: 40 mg every other week
2. Uveitis
   a. Prescriber will be dosing the patient within the FDA labeled maintenance dose of the following:
      i. Age 2-17, weight 10kg to < 15kg: 10 mg every other week
      ii. Age 2-17, weight 15kg to < 30kg: 20 mg every other week
      iii. Age 2-17, weight ≥30kg: 40 mg every other week
      iv. Age 18 and older: 40 mg every other week

Age 5 years of age or older

1. Ulcerative Colitis (UC)
   a. Prescriber will be dosing the patient within the FDA labeled maintenance dose of the following:
      i. Age 5-17, weight 20kg to <40kg: 40 mg every other week or 20 mg every week
      ii. Age 5-17, weight ≥40kg: 80 mg every other week or 40 mg every week
      iii. Age 18 and older: 40 mg every other week **OR** 20 mg every week, or 40 mg every week/80 mg every other

week if patient was established and stable on pediatric dosing regimen

Age 6 years of age or older

1. Crohn's Disease (CD)
    a. Prescriber will be dosing the patient within the FDA labeled maintenance dose of the following:
        i. Age 6-17, weight 17kg to < 40kg: 20 mg every other week
        ii. Age 6-17, weight ≥40kg: 40 mg every other week
        iii. Age 18 and older: 40 mg every other week

Age 12 years of age or older

1. Rheumatoid Arthritis (RA)
    a. Prescriber will be dosing the patient within the FDA labeled maintenance dose of the following:
        i. Concurrent therapy with methotrexate: 40 mg every other week
        ii. **NO** concurrent therapy with methotrexate: 40 mg every week or 80 mg every other week
2. Psoriatic Arthritis (PsA)
    a. Prescriber will be dosing the patient within the FDA labeled maintenance dose of 40 mg every other week
3. Ankylosing Spondylitis (AS)
    a. Prescriber will be dosing the patient within the FDA labeled maintenance dose of 40 mg every other week
4. Plaque Psoriasis (PsO)
    a. Prescriber will be dosing the patient within the FDA labeled maintenance dose of 40 mg every other week
5. Hidradenitis Suppurativa (HS)
    a. Prescriber will be dosing the patient within the FDA labeled maintenance dose of the following:
        i. Age 12-17, weight 30 kg to <60kg: 40 mg every other week
        ii. Age 12-17, weight ≥60kg: 40 mg every week or 80 mg every other week

iii. Age 18 and older: 40 mg every week or 80 mg every other week

AND ALL of the following:

a. Condition has improved or stabilized with Humira
b. Absence of active infection [including tuberculosis and hepatitis B virus (HBV)]
c. **NOT** to be used in combination with any other biologic DMARD or targeted synthetic DMARD (see Appendix 1)
d. **NOT** given concurrently with live vaccines

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Diagnosis	Starter Pack	Strength	Quantity
Rheumatoid Arthritis	No	40 mg/0.4 mL 40 mg/0.8 mL 80 mg/0.8mL	**NO** concurrent methotrexate: 12 x 40mg units per 84 days **OR** 6 x 80mg units per 84 days **OR** Concurrent methotrexate: 6 x 40mg units per 84 days
Psoriatic Arthritis	No	40 mg/0.4 mL 40 mg/0.8 mL	6 x 40mg units per 84 days
Ankylosing Spondylitis	No	40 mg/0.4 mL 40 mg/0.8 mL	6 x 40mg units per 84 days
Plaque Psoriasis	***Yes***	40 mg/0.4 mL 40 mg/0.8 mL	1 Starter Pack **and** 6 x 40mg units per 84 days
Ulcerative Colitis	***Yes***	**Age 5-17 (20 kg to < 40kg)** 20 mg/0.2 mL 20 mg/0.4 mL 40 mg/0.4 mL 40 mg/0.8 mL	1 Starter Pack **and** 12 x 20mg units per 84 days **OR** 6 x 40mg units per 84 days
		Age 5-17 (≥ 40 kg) 40 mg/0.4 mL 40 mg/0.8 mL 80 mg/0.8mL	1 Starter Pack **and** 12 x 40mg units per 84 days **OR** 6 x 80mg units per 84 days

		Age 18+: 20 mg/0.2 mL 20 mg/0.4 mL 40 mg/0.4 mL 40 mg/0.8 mL 80 mg/0.8mL	1 Starter Pack **and** 6 x 40mg units per 84 days **OR** **Pediatric patients who turn 18 years of age and are well-controlled on their Humira regimen:** 12 x 20 mg units per 84 days **OR** 12 x 40 mg units per 84 days **OR** 6 x 40mg units per 84 days **OR** 6 x 80 mg units per 84 days
Crohn's Disease	***Yes***	**Age 6-17 (17 kg to < 40kg)** 20 mg/0.2 mL 20 mg/0.4 mL	1 Starter Pack **and** 6 x 20mg units per 84 days **OR**
		Age 6-17 (≥ 40kg) 40 mg/0.4 mL 40 mg/0.8 mL	1 Starter Pack **and** 6 x 40mg units per 84 days
		Age 18+: 40mg/0.4 mL 40 mg/0.8 mL	1 Starter Pack **and** 6 x 40mg units per 84 days
Polyarticular Juvenile Idiopathic Arthritis (pJIA)	No	**Age 2+ (10 kg to < 15 kg)** 10 mg/0.1 mL 10 mg/0.2 mL	6 x 10mg units per 84 days
		Age 2+ (15 kg to < 30 kg) 20 mg/0.2 mL 20 mg/0.4 mL	6 x 20mg units per 84 days
		Age 2+ (≥ 30 kg) 40 mg/0.4 mL 40 mg/0.8 mL	6 x 40mg units per 84 days
Uveitis	No	**Age 2-17 (10 kg to < 15 kg)** 10 mg/0.1 mL 10 mg/0.2 mL	6 x 10mg units per 84 days
		Age 2-17 (15 kg to < 30 kg) 20 mg/0.2 mL 20 mg/0.4 mL	6 x 20mg units per 84 days
		Age 2-17 (≥ 30 kg) 40 mg/0.4 mL 40 mg/0.8 mL	6 x 40mg units per 84 days
	Yes	**Age 18+:** 40 mg/0.4 mL 40 mg/0.8 mL	1 Starter Pack **and** 6 x 40mg units per 84 days

Hidradenitis Suppurativa	***Yes***	**Age 12-17 (30 kg to < 60 kg)** 40 mg/0.4 mL 40 mg/0.8 mL	1 Starter Pack **and** 6 x 40mg units per 84 days
		Age 12-17 (≥ 60 kg) 40 mg/0.4 mL 40 mg/0.8 mL 80mg/0.8mL	1 Starter Pack **and** 12 x 40mg units per 84 days **OR** 6 x 80mg units per 84 days
		Age 18+: 40 mg/0.4 mL 40 mg/0.8 mL 80 mg/0.8mL	1 Starter Pack **and** 12 x 40mg units per 84 days **OR** 6 x 80mg units per 84 days

Duration 12 months

Prior – Approval *Renewal* Limits

Quantity

Diagnosis	Strength	Quantity
Rheumatoid Arthritis	40 mg/0.4 mL 40 mg/0.8 mL 80 mg/0.8mL	**NO** concurrent methotrexate: 12 x 40mg units per 84 days **OR** 6 x 80mg units per 84 days **OR** Concurrent methotrexate: 6 x 40mg units per 84 days
Psoriatic Arthritis	40 mg/0.4 mL 40 mg/0.8 mL	6 x 40mg units per 84 days
Ankylosing Spondylitis	40 mg/0.4 mL 40 mg/0.8 mL	6 x 40mg units per 84 days
Plaque Psoriasis	40 mg/0.4 mL 40 mg/0.8 mL	6 x 40mg units per 84 days
Ulcerative Colitis	**Age 5-17 (20 kg to < 40kg)** 20 mg/0.2 mL 20 mg/0.4 mL 40 mg/0.4 mL 40 mg/0.8 mL	12 x 20mg units per 84 days **OR** 6 x 40mg units per 84 days
	Age 5-17 (≥ 40 kg) 40 mg/0.4 mL 40 mg/0.8 mL 80 mg/0.8mL	12 x 40mg units per 84 days **OR** 6 x 80mg units per 84 days
	Age 18+: 20 mg/0.2 mL 20 mg/0.4 mL 40 mg/0.4 mL	6 x 40mg units per 84 days **OR** **Pediatric patients who turn 18 years of age and are well-**

	40 mg/0.8 mL 80 mg/0.8mL	**controlled on their Humira regimen:** 12 x 20mg units per 84 days **OR** 12 x 40mg units per 84 days **OR** 6 x 40mg units per 84 days **OR** 6 x 80mg units per 84 days
Crohn's Disease	**Age 6-17 (17 kg to < 40kg)** 20 mg/0.2 mL 20 mg/0.4 mL	6 x 20mg units per 84 days
	Age 6-17 (≥ 40kg) 40 mg/0.4 mL 40 mg/0.8 mL	6 x 40mg units per 84 days
	Age 18+: 40mg/0.4 mL 40 mg/0.8 mL	6 x 40mg units per 84 days
Polyarticular Juvenile Idiopathic Arthritis (pJIA)	**Age 2+ (10 kg to < 15 kg)** 10 mg/0.1 mL 10 mg/0.2 mL	6 x 10mg units per 84 days
	Age 2+ (15 kg to < 30 kg) 20 mg/0.2 mL 20 mg/0.4 mL	6 x 20mg units per 84 days
	Age 2+ (≥ 30 kg) 40 mg/0.4 mL 40 mg/0.8 mL	6 x 40mg units per 84 days
Uveitis	**Age 2-17 (10 kg to < 15 kg)** 10 mg/0.1 mL 10 mg/0.2 mL	6 x 10mg units per 84 days
	Age 2-17 (15 kg to < 30 kg) 20 mg/0.2 mL 20 mg/0.4 mL	6 x 20mg units per 84 days
	Age 2-17 (≥ 30 kg) 40 mg/0.4 mL 40 mg/0.8 mL	6 x 40mg units per 84 days
	Age 18+: 40 mg/0.4 mL 40 mg/0.8 mL	6 x 40mg units per 84 days
Hidradenitis Suppurativa	**Age 12-17 (30 kg to < 60 kg)** 40 mg/0.4 mL 40 mg/0.8 mL	6 x 40mg units per 84 days
	Age 12-17 (≥ 60 kg) 40 mg/0.4 mL 40 mg/0.8 mL 80mg/0.8mL	12 x 40mg units per 84 days **OR** 6 x 80mg units per 84 days
	Age 18+: 40 mg/0.4 mL	12 x 40mg units per 84 days **OR** 6 x 80mg units per 84 days

	40 mg/0.8 mL 80 mg/0.8mL	

Duration 18 months

Rationale

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 (1-26).

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

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.; July 2022.
4. Cyltezo [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; August 2017.
5. Hyrimoz [package insert]. Princeton, NJ: Sandoz Inc.; July 2022.
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 2022.
9. Yusimry [package insert]. Redwood City, CA: Coherus BioSciences, Inc.; December 2021.
10. Idacio [package insert]. Lake Zurich, IL: Fresenius Kabi USA, LLC; December 2022.
11. Yuflyma [package insert].Jersey City, NJ: Celltrion USA, Inc.; May 2023.

12. 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.
13. Sulpice M et al. Efficacy and safety of anti-TNF alpha therapy in patients with juvenile spondyloarthropathy. Joint Bone Spine 2009;76:24.
14. Sieper J et al. Adalimumab for treatment of ankylosing spondylitis . Expert Opin Pharmacother 2007;8:831.
15. Tse SM et al. Anti-TNF alpha blockade in treatment of juvenile spondyloarthropathy. Arthritis Rheum 2005;52:2103.
16. 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.
17. Saeed SA, Crandall WV. Managing Crohn's disease in children and adolescents: focus on TNF antagonists. Paediatr Drugs 2008;10:31-38.
18. Noe JD, Pfeffakorn M. Short-term response to Adalimumab in childhood inflammatory bowel disease. Inflam Bowel Dis 2008;14:1683-87.
19. 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.
20. 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.
21. Evers EA et al. Factors predictive of Crohn disease following colectomy in medically refractory pediatric colitis. J Pediatr Gastroenterol Nutr 2009;48:283-286.
22. 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].
23. 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.
24. 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].
25. Smita V. Sukhatme, Alice B. Gottlieb. Pediatric psoriasis: updates in biologic therapies. Dermatologic Therapy. Volume 22, Issue 1, pages 34–39, January/February 2009.
26. Dermatology. Jean Bolognia, et al. 3rd edition. Philadelphia, PA: Saunders, Inc.; 2012.
27. Biosimilar and Interchangeable Products. U.S. Food & Drug Administration. October 23, 2017. Accessed February 2021. https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandAppr

oved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm580419.htm#generic

Policy History

Date	Action
October 2013	Addition to PA
December 2013	Annual editorial review by the PMPC
September 2014	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
October 2014	Age limit lowered to 2 and older for PJIA
December 2014	Annual editorial review and reference update
June 2015	Annual review and reference update
August 2015	Addition of off-Label indications: uvetis and hidradenitis suppurativa (HS)
December 2015	Annual review and reference update
September 2016	Annual editorial review and reference update Addition of not to be used in combination with any other biologic DMARD or targeted synthetic DMARD Addition of not given concurrently with live vaccines per SME Policy number change from 5.18.01 to 5.70.29
October 2016	Addition of Amjevita (biosimilar) to criteria
December 2016	Annual review and reference update
March 2017	Annual review
June 2017	Annual review
December 2017	Annual review
March 2018	Annual editorial review and reference update Addition of Appendix 1 - List of DMARDs

June 2018	Annual editorial review Addition of Appendix 2 - List of Conventional Therapies and Appendix 3 - Examples of Contraindications to Methotrexate Addition of additional requirements to initiation criteria For diagnoses of RA and pJIA: inadequate treatment response, intolerance, or contraindication to at least ONE conventional disease-modifying antirheumatic drugs (DMARDs) For diagnoses of UC and CD: inadequate treatment response, intolerance, or contraindication to at least one conventional systemic therapy For diagnosis of AS: inadequate response, intolerance, or contraindication to at least 2 NSAIDs For diagnosis of PsA: inadequate response, intolerance or contraindication to a 3-month trial of at least ONE conventional DMARD For diagnosis of PsO: if the patient is intolerant or contraindicated to either therapy then the other treatment option needs to be tried
September 2018	Annual editorial review and reference update Change of age limit for uveitis to 2 years and older Addition of off-label indications to Amjevita per SME
November 2018	Annual review and reference update. Addition of Cyltezo and Hyrimoz (biosimilars) to criteria
March 2019	Annual review and reference update
August 2019	Addition of biosimilar Hadlima
September 2019	Annual review
December 2019	Annual review and reference update. Addition of biosimilar Abrilada
March 2020	Annual review
August 2020	Addition of biosimilar Hulio
September 2020	Annual review
December 2020	Added requirements to dose within the FDA labeled maintenance dosing. Added PA quantity limits
January 2021	Updated maintenance dose for RA not receiving methotrexate and HS from 40mg every week to 40mg every week or 80 mg every other week
March 2021	Annual editorial review and reference update. Revised age requirement for ulcerative colitis from 12 and older to 5 and older. Revised ulcerative colitis dosing requirement for adult patients. Updated dosing charts. Appendix 1 updated.
June 2021	Annual review
January 2022	Addition of biosimilar Yusimry
March 2022	Annual review
September 2022	Annual review and reference update
December 2022	Annual review
January 2023	Addition of biosimilar Idacio
March 2023	Annual review
June 2023	Annual review. Addition of biosimilar Yuflyma

December 2023	Annual review. Per FEP, revised preferred products to Humira, Hyrimoz, adalimumab-adaz, and adalimumab-fkjp

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.

Appendix 1 - List of DMARDs

Conventional disease-modifying antirheumatic drugs (DMARDs)

Generic Name	Brand Name
azathioprine	Azasan, Imuran
cyclophosphamide	Cytoxan
cyclosporine	Neoral, Gengraf, Sandimmune
hydroxychloroquine	Plaquenil
leflunomide	Arava
methotrexate	Rheumatrex, Trexall
mycophenolate	Cellcept
sulfasalazine	Azulfidine, Sulfazine

Biological disease-modifying antirheumatic drugs (DMARDs)

Generic Name	Brand Name
abatacept	Orencia
adalimumab	Humira
anakinra	Kineret
brodalumab	Siliq
certolizumab	Cimzia
etanercept	Enbrel
golimumab	Simponi/Simponi Aria
guselkumab	Tremfya
infliximab	Remicade/Avsola/Inflectra/Renflexis
ixekizumab	Taltz
risankizumab-rzaa	Skyrizi
rituximab	Rituxan/Riabni/Ruxience/Truxima
sarilumab	Kevzara
secukinumab	Cosentyx
spesolimab-sbzo	Spevigo
tildrakizumab-asmn	Ilumya
tocilizumab	Actemra
ustekinumab	Stelara
vedolizumab	Entyvio

Targeted synthetic disease-modifying antirheumatic drugs (DMARDs)

Generic Name	Brand Name
apremilast	Otezla
baricitinib	Olumiant
deucravacitinib	Sotyktu

tofacitinib	Xeljanz/XR
upadactinib	Rinvoq

Appendix 2 - List of Conventional Therapies

Conventional Therapy Options for CD
1. Mild to moderate disease – induction of remission: a. Oral budesonide, oral mesalamine b. Alternatives: metronidazole, ciprofloxacin
2. Mild to moderate disease – maintenance of remission: a. Azathioprine, mercaptopurine b. Alternatives: oral budesonide, methotrexate intramuscularly (IM)
3. Moderate to severe disease – induction of remission: a. Prednisone, methylprednisolone intravenously (IV) b. Alternatives: methotrexate IM
4. Moderate to severe disease – maintenance of remission: a. Azathioprine, mercaptopurine b. Alternative: methotrexate IM
5. Perianal and fistulizing disease – induction of remission c. Metronidazole ± ciprofloxacin
6. Perianal and fistulizing disease – maintenance of remission d. Azathioprine, mercaptopurine e. Alternative: methotrexate IM

Conventional Therapy Options for UC
1. Mild to moderate disease – induction of remission: a. Oral mesalamine (e.g., Asacol, Lialda, Pentasa), balsalazide, olsalazine b. Rectal mesalamine (e.g., Canasa, Rowasa) c. Rectal hydrocortisone (e.g., Colocort, Cortifoam) d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission: a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission: a. Prednisone, hydrocortisone IV, methylprednisolone IV b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission: a. Azathioprine, mercaptopurine b. Alternative: sulfasalazine
5. Pouchitis: a. Metronidazole, ciprofloxacin b. Alternative: rectal mesalamine

Appendix 3 – Examples of Contraindications to Methotrexate

Contraindications to Methotrexate
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction