Subject: **Anti -Tumor Necrosis Factor (TNF) Therapy(adalimumab, etanercept, certolizumab, golimumab, infliximab) ***

Effective Date:

Department: **Utilization Management**

Policy: Injectable ant-TNF therapy is reimbursable under plans administered by QualCare, Inc. for client groups whose pharmacy benefit excludes specified injectable biologic therapies when an eligible member benefit is in place and medical necessity exists.

Objective: To assure consistent reimbursement for injectable Infliximab as a medically necessary service and to delineate criteria that provides evidence of that Medical necessity.

Procedure: Requests for coverage of injectable anti-TNF therapy must be applied against criteria below.

Definition: Anti-TNF agents are injectable, (subcutaneously or intravenously infused), chimeric monoclonal antibodies or receptor fusion protein (etanercept) that bind to tumor necrosis factor alpha (TNF-a). It is believed to be critical to the human body's reaction to inflammation. TNF-a is a cytokine that is a key biologic response mediator found to be increased in chronic and inflammatory disorders such as Crohn's disease, rheumatoid arthritis (RA), and other autoimmune diseases.

Brand Names: available anti-TNF agents are

- Adalimumab (Humira®)
- Certolizumab (Cimzia®)
- Etanercept (Enbrel®)
- Golimumab (Simponi®)- subcutaneous version
- Golumimab (Simponi Aria®)- intravenous version
- Infliximab (Remicade®)

Criteria: Condition-specific criteria for anti-TNF therapy are specified below:

A. Rheumatologic Disorders

Diagnosis	Coverable anti-TNF Drugs	Criteria for Use
Ankylosing Spondylitis(AS)[ICD-10 M45.0-M45.9] **Reactive Arthritis [ICD-10 M02.81-M02.9]**	Adalimumab, certolizumab, etanercept, golimumab, infliximab	failure or inadequate response, contraindication per FDA label, or documented intolerance to at least ONE non-steroidal anti-inflammatory drug (NSAIDs) for at least 4 weeks. Additionally, for reactive arthritis, inadequate response, contraindication or intolerance to sulfasalazine for at least four months.
Polyarticular Juvenile Idiopathic Arthritis (PJIA) [ICD-10 M08.0, M08.9, M08.29,]	Adalimumab and etanercept in a child ≥ 2 years of age. Infliximab in a child ≥ 6 years of age.	Confirmed diagnosis of polyarticular juvenile idiopathic arthritis(PJIA) and inadequate response to 3 months of methotrexate or lefluonamide therapy.
Psoriatic Arthritis (PsA) [ICD-10 L40.50-L40.50]	Adalimumab, certolizumab, etanercept, golimumab, infliximab	failure or inadequate response, contraindication per FDA label, or documented intolerance to one NSAID AND methotrexate

Rheumatoid Arthritis(RA) [ICD-10 M05-M05.331, M06-M06.9]	Adalimumab,certolizumab,etanercept, golimumab(SC and IV forms), infliximab.	RA in an adult, with failure or inadequate response, contraindication per FDA label, or documented intolerance to at least ONE disease-modifying anti-rheumatic drug (DMARD) (e.g., methotrexate**,** leflunomide, sulfasalazine). NOTE: Golumab and infliximab require use in combination with methotrexate (unless contraindicated per FDA label or documented intolerance)

B. Gastrointestinal Disorders

Crohn's Disease (CD) –Adult [ICD-10 K50- K50.919]	Adalimumab, certolizumab, infliximab	active CD with failure or inadequate response, contraindication per FDA label, or documented intolerance to at least ONE conventional therapy (i.e., aminosalicylate, corticosteroids, or immumomodulators such as azathioprine, 6-mercaptopurine, or methotrexate); OR infliximab is approvable for fistulizing Crohn's disease with fistula present for at least three (3) months in duration
Crohn's Disease (CD) – Pediatric [ICD-10 K50-K50.919]	Adalimumab, infliximab	active CD in a child ≥ 6 years of age with failure or inadequate response, contraindication per FDA label, or documented intolerance, to at least ONE conventional therapy (i.e., aminosalicylate, corticosteroids, or immumomodulators) **OR**

		for infliximab, a history of beneficial clinical response to infliximab.
Ulcerative Colitis (UC)- Adult [ICD-10 K51-K51.919]	Adalimumab, golimumab(SC), infliximab	Active UC with failure or inadequate response, contraindication per FDA label or documented intolerance to at least ONE conventional therapy: (i.e., aminosalicylate, corticosteroids or immunomodulators)
Ulcerative Colitis- Pediatric [ICD-10 K51-K51.919]	infliximab	Active UC in a child ≥ 6 years of age with failure or inadequate response, contraindication per FDA label, or documented intolerance to at least ONE conventional therapy (i.e. aminosalicylate, corticosteroids, or immumomodulators)

C. Dermatologic Disorders

Chronic Plaque Psoriasis [ICD-10 L40-L40.9]	Adalimumab, etanercept, infliximab	chronic plaque psoriasis (> 1 year duration) in an adult with > 10% of body surface area affected AND failure or inadequate response, contraindication per FDA label, or documented intolerance to ANY of the following: • Systemic therapy (e.g., methotrexate, cyclosporine, Soriatane) • Phototherapy [narrow or broad band ultraviolet B (UVB), or psoralen plus ultraviolet A (PUVA)]

		• Topical therapy (e.g., coal tar, keratolytics, corticosteroids, anthralin, Dovonex**,** Tazorac**)**
Hidradenitis Suppurativa [ICD-10 L73.2]]	adalimumab	Diagnosis of moderate to severe hidradenitis suppurativa (Hurley Stage II or III disease) and with at least 3 abscesses or inflammatory nodules AND failure of conventional medical management (e.g. good hygiene, antibiotic therapy, and surgical incision & drainage)

D. Ophthalmologic Conditions

Diagnosis	Coverable Anti-TNF Drugs	Criteria for Use
Bechet's Uveitis [ICD-10 H20, H20.9]	Adalimumab, infliximab	Active Bechet's uveitis with failure or inadequate response, contraindication per FDA label, or documented intolerance to conventional therapy (such as corticosteroids or immunosuppressive drugs [for example, azathioprine, cyclosporine, or methotrexate])

Authorization parameters – when the criteria for use in this policy are met for the specific drug and diagnosis an authorization can be approved for one year period, with renewal of the authorization upon documentation of continued clinical response.

E. FDA Recommended Dosing (unless noted as off-label)

DRUG	DIAGNOSIS	DOSING
Adalimumab(Humira®) (subcutaneous injection)	Adults with Ankylosing Spondylitis/Reactive Arthritis(off-label), Psoriatic arthritis, rheumatoid arthritis	40mg every other week
	Crohn's Disease -Adults	160mg initially, then 40 mg 2 weeks later, followed 2 weeks later by 40 mg every other week
	Crohn's Disease-Pediatric	For body weight 17 kg (37 lbs) to < 40 kg (88 lbs): 80 mg on Day 1 followed by 40 mg two weeks later followed in 2 weeks by 20 mg every other week. For body weight ≥ 40 kg (88 lbs) 160 mg on Day 1 followed by 80 mg two weeks later followed in 2 weeks by 40 mg every other week
	Juvenile Idiopathic Arthritis	For body weight 10 kg (22 lbs) to <15 kg (33 lbs): 10 mg every other week For body weight 15 kg (33 lbs) to <30 kg (66 lbs): 20 mg every other week For body weight ≥30 kg (66 lbs): 40 mg every other week
	Chronic Plaque Psoriasis	80 mg initial dose, then 40 mg every other week
	Ulcerative Colitis	160 mg initial dose, with 80 mg 2 weeks later, followed in 2 weeks by 40 mg every other week.
Certolizumab (Cimzia®) (subcutaneous injection)	Ankylosing Spondylitis	400 mg at 0,2 and 4 weeks, then 200 mg every two weeks or 400 mg every four weeks.

Certolizumab (Cimzia®)	Crohn's Disease	400 mg at 0,2 and 4 weeks, then 400 mg every four weeks
	Psoriatic Arthritis Rheumatoid Arthritis	400 mg at 0,2 and 4 weeks, then 200 mg every other weeks or 400 mg every four weeks
Etanercept (Enbrel®) (subcutaneous)	Adults with Rheumatoid Arthritis, Psoriatic Arthritis and Ankylosing Spondylitis	50 mg once weekly or 25 mg twice weekly.
	Juvenile Idiopathic Arthritis	Weight based- 0.8mg/kg per week up to 50 mg per week maximum.
	Plaque Psoriasis	50 mg twice weekly for the first three months, followed by 50 mg once weekly.
Golimumab (Simponi®) (subcutaneous)	Ankylosing Spondylitis, Psoriatic Arthritis, Rheumatoid Arthritis	50 mg once a month.
	Ulcerative Colitis	200mg initial dose, then 100 mg at week 2, followed by 100 mg every four weeks.
Golimumab (Simponi Aria®) (intravenous)	Rheumatoid Arthritis	Weight based- 2mg/kg initial and at week 4, then every eight weeks.
Infliximab (Remicade®) (Intravenous)	Ankylosing Spondylitis, Reactive arthritis (off -label),Plaque Psoriasis, Psoriatic Arthritis, Psoriasis Juvenile idiopathic arthritis(JIA) (off-label)	Weight based- 5 mg/kg at 0,2 and 6 weeks followed by 5 mg/kg every eight weeks For JIA- weight based- 3mg/kg at 0,2 and6 weeks , followed by 3 to 6 mg/kg every eight weeks
	Crohn's Disease or Fistulizing Crohn's Disease	Weight based- 5 mg/kg at 0,2 and 6 weeks followed by 5 mg/kg every eight weeks up to a maximum of 10mg/kg if response is lost to lower dosing.

Infliximab(Remicade®) (intravenous)	Pediatric Crohn's Disease	Weight based- 5 mg/kg at 0,2 and 6 weeks followed by 5 mg/kg every eight weeks
	Rheumatoid Arthritis	Weight based- 3mg/kg at 0,2 and 6 weeks followed by 3mg/kg every eight weeks, up to 10 mg/kg if there is incomplete response to lower dosing.

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This policy incorporates retired policy "Injectable Infliximab("Remicade").

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*Consistent with Summary Plan Description (SPD). When there is discordance between this policy and the SPD, the provisions of the SPD prevail.