BlueCross BlueShield of Arizona

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PHARMACY COVERAGE GUIDELINES	ORIGINAL EFFECTIVE DATE:	4/1/19
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BIOLOGIC AND IMMUNOLOGICAL AGENTS

ACTEMRA® (tocilizumab) intravenous and subcutaneous injection (IV&SQ)
CIMZIA® (certolizumab pegol) subcutaneous injection
COSENTYX® (secukinumab) subcutaneous injection
ENBREL® (etanercept) subcutaneous injection
HUMIRA® (adalimumab) subcutaneous injection
KEVZARA® (sarilumab) subcutaneous injection
KINERET® (anakinra) subcutaneous injection
ORENCIA® (abatacept) intravenous and subcutaneous injection (IV&SQ)
OTEZLA® (apremilast) oral tablet
RITUXAN® (rituximab) intravenous solution
SILIQ™ (brodalumab) subcutaneous injection
SIMPONI® (golimumab) subcutaneous injection
SIMPONI ARIA® (golimumab) intravenous solution
STELARA® (ustekinumab) intravenous and subcutaneous injection (IV&SQ)
TALTZ® (ixekizumab) subcutaneous injection
TREMFYA® (guselkumab) subcutaneous injection
XELJANZ® (tofacitinib citrate) oral tablet
XELJANZ® XR (tofacitinib citrate) extended-release tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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BIOLOGIC AND IMMUNOLOGICAL AGENTS (cont.)

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

Section A. Applies for all indications and uses:

- **Criteria for initial therapy:** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in or is in consultation with a Rheumatologist, Dermatologist, Gastroenterologist, or Ophthalmologist, depending upon indication or use

  2. Meets other initial criteria per indication or use as described below in Sections B-N below

  3. **ONE** of the following for Hepatitis B:
     - Individual is negative for Hepatitis B demonstrated by negative HBsAg or HBcAb
     - Individual with known Hepatitis B carriers have concurrent treatment with antiviral therapy or is monitored closely for reactivation
     - **For Otezla**: Does not apply

  4. There is no evidence of active serious infections, including clinically important localized infections or sepsis when initiating or continuing therapy **(Does not apply for Otezla)**

  5. Individual does not have untreated latent or active tuberculosis **(Does not apply for Otezla)**

  6. There is no concurrent use of live vaccines **(Does not apply for Otezla)**

  7. There is no concurrent use with other biologic and immunologic agents

  8. There are no significant interacting drugs

- **Criteria for continuation of coverage (renewal request):** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by a physician specializing in or is in consultation with a Rheumatologist, Dermatologist, Gastroenterologist, or Ophthalmologist depending upon indication or use

2. Meets other continuation criteria per indication or use as described in Sections B-N below

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use

5. **ONE** of the following for Hepatitis B:
   - Individual is negative for Hepatitis B demonstrated by negative HBsAg or HBcAb
   - Individual with known Hepatitis B carriers have concurrent treatment with antiviral therapy or is monitored closely for reactivation
   - **For Otezla**: Does not apply

6. There is no evidence of active serious infections, including clinically important localized infections or sepsis when initiating or continuing therapy **(Does not apply for Otezla)**

7. Individual does not have untreated latent or active tuberculosis **(Does not apply for Otezla)**

8. Individual with a history of heart failure is monitored closely for symptoms of heart failure while on therapy

9. There is no evidence of lupus-like syndrome while on therapy

10. There is no concurrent use of live vaccines **(Does not apply for Otezla)**

11. There is no concurrent use with other biologic and immunologic agents

12. There are no significant interacting drugs

Section B. Moderately to severely active Rheumatoid Arthritis (RA):

- **Criteria for initial therapy** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met for moderately to severely active rheumatoid arthritis:

1. Request is for **ONE** of the following: Actemra (SC), Cimzia, Enbrel, Humira, Kevzara, Kineret, Orencia (IV&SQ), Rituxan, Simponi, Simponi Aria, Xeljanz IR, Xeljanz XR

2. Prescriber is a Rheumatologist

3. Meets other initial criteria per indication or use as described in Section A above

4. Individual is 18 years of age or older

5. Diagnosis of rheumatoid arthritis identified by **ONE** of the following:

- Clinical Disease Activity Index (CDAI) score greater than 10
- Disease Activity Score 28 (DAS28) of greater than 3.2
- Patient Activity Scale (PAS) of greater than 3.7
- Patient Activity Scale II (PASII) of greater than 3.7
- Routine Assessment of Patient Index Data 3 (RAPID-3) score greater than 2
- Simplified Disease Activity Index (SDAI) score greater than 11

6. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **methotrexate** and **ONE or more** of the following (unless individual has already failed another TNF-inhibitor):
   - Leflunomide
   - Sulfasalazine

7. For **non-preferred agents** for rheumatoid arthritis:

   Kevzara:
   - Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **TWO** of the following preferred agents:
     - Cimzia
     - Humira
     - Simponi and Simponi Aria

   Actemra, Enbrel, Kineret, Orencia (IV&SQ), Rituxan:
   - **ALL** of the following:
     - Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **TWO** of the following preferred agents:
       - Cimzia
       - Humira
       - Simponi and Simponi Aria
     - Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **BOTH** of the following:
       - Kevzara
       - Xeljanz IR or Xeljanz XR

   Xeljanz IR or Xeljanz XR:
   - Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **TWO** of the following preferred agents:
     - Cimzia
     - Humira
     - Simponi and Simponi Aria

8. **For Actemra**, absolute neutrophil count 2,000/mm^3 or greater, ALT and AST levels 1.5 X ULN, platelet count 100 $x10^9$/L or greater

Approval Duration: 6 months all agents except for Rituxan
Rituxan: Total of 3 infusions of 1000 mg over 6 months

BIOLOGIC AND IMMUNOLOGICAL AGENTS (cont.)

- **Criteria for continuation of coverage (renewal request):** Biologic and Immunological Agents considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Meets other continuation criteria as described in Section A above

  2. Individual's condition responded while on therapy
     - Response is defined as AT LEAST a 20% improvement in any of the following: CDAI, DAS28, PAS, PASII, RAPID-3, SDAI (see Definition section)

  Renewal Duration: 12 months all agents except for Rituxan
  Rituxan: 2 infusions of 1000 mg each over 12 months

Section C. Moderately to severely active Psoriatic Arthritis (PsA):

- **Criteria for initial therapy:** Biologic and Immunological Agents considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met for moderately to severely active psoriatic arthritis:

  1. Request is for **ONE** of the following: Cimzia, Cosentyx, Enbrel, Humira, Orencia (IV&SQ), Otezla, Simponi, Stelara, Taltz, Xeljanz IR, Xeljanz XR

  2. Prescriber is a Rheumatologist

  3. Meets other initial criteria per indication or use as described in Section A above

  4. Individual is 18 years of age and older

  5. Diagnosis of moderate to severe active psoriatic arthritis is identified by **ONE or more** of the following:
     - Predominantly axial disease (i.e. sacroiliitis or spondylitis) as indicated by **ALL** of the following:
       - Radiographic evidence of axial disease (e.g., sacroiliac joint space narrowing or erosions, vertebral syndesmophytes)
       - Symptoms (e.g., limited spinal range of motion, spinal morning stiffness more than 30 minutes) present for more than 3 months' duration
       - Failure or intolerance of 2 or more different NSAIDs (at maximum recommended doses) over total period of at least 4 or more weeks of therapy

     - Predominantly non-axial disease, and failure of, intolerance to, or contraindication to both methotrexate and NSAIDs

  6. For **non-preferred agents** for psoriatic arthritis:

     Cosentyx, Xeljanz IR or Xeljanz XR:
     - Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **TWO** of the following preferred agents:
       - Cimzia
       - Humira
       - Otezla

- Simponi and Simponi Aria
- Stelara

Enbrel, Orencia (IV&SQ), Taltz:

- **ALL** of the following:
  - Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **TWO** of the following preferred agents:
    - Cimzia
    - Humira
    - Simponi or Simponi Aria
    - Stelara
  - Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **BOTH** of the following:
    - Cosentyx
    - Xeljanz IR or Xeljanz XR

Approval Duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Meets other continuation criteria as described in Section A above
2. Individual's condition responded while on therapy
   - Response is defined as AT LEAST a 20% improvement in any of the following: CDAI, DAS28, PAS, PASII, RAPID-3, SDAI (see Definition section)

Renewal Duration: 12 months

Section D. Moderately to severely active Ankylosing Spondylitis (AS):

- **Criteria for initial therapy:** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met for moderately to severely active ankylosing spondylitis:

1. Request is for **ONE** of the following: Cimzia, Cosentyx, Enbrel, Humira, Simponi, Simponi Aria
2. Prescriber is a Rheumatologist
3. Meets other initial criteria per indication or use as described in Section A above
4. Individual is 18 years of age or older
5. Clinical and diagnostic imaging evidence of ankylosing spondylitis as indicated by **ALL** of the following:
   - Back pain of 3 months or more duration and age of onset of 45 years or younger

BIOLOGIC AND IMMUNOLOGICAL AGENTS (cont.)

- Sacroiliitis on imaging
- Spondyloarthritis signs or symptoms as indicated by **ONE or more** of the following:
  - Arthritis
  - Elevated serum C-reactive protein
  - Enthesitis (e.g., inflammation of Achilles tendon insertion)
  - HLA-B27
  - Limited chest expansion
  - Morning stiffness for one hour or more

6. Disease activity and treatment scenario as indicated by **ONE or more** of the following:
   - Axial (spinal) disease
   - Failure of or intolerance to treatment with anti-tumor necrosis factor-alpha drug
   - Peripheral arthritis without axial involvement, and failure or intolerance of 4 or more months of therapy with sulfasalazine

7. Individual has failure, contraindication or intolerance to **TWO or more** different NSAIDs (at maximum recommended doses) over a total period of at least 4 or more weeks of therapy

8. For **non-preferred agents** for ankylosing spondylitis:
   Cosentyx, Enbrel:
   - Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **TWO** of the following preferred agents:
     - Cimzia
     - Humira
     - Simponi or Simponi Aria

   Approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Meets other continuation criteria as described in Section A above

  2. Individual's condition responded while on therapy
     - Response is defined as AT LEAST a 20% improvement in BASDAI (see Definition section)

  Renewal Duration: 12 months

Section E. Moderately to severely active Crohn's Disease (CD):

- **Criteria for initial therapy:** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met for moderately to severely active Crohn's disease:

  1. Request is for **ONE** of the following: Cimzia, Humira, Stelara

  2. Prescriber is a Gastroenterologist

3. Meets other initial criteria per indication or use as described in Section A above

4. Age of individual meets FDA-approved label

5. Diagnosis of moderate to severe active Crohn disease as indicated by **ONE or more** of the following:
   - Abdominal abscess
   - Anemia
   - Dehydration
   - Elevated serum C-reactive protein level
   - Fever
   - Intermittent vomiting
   - Intestinal obstruction
   - Weight loss of greater than 10% of body weight

6. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **ONE or more** of the following:
   - 6-mercaptopurine
   - Azathioprine
   - Methotrexate
   - Oral corticosteroids

   Approval Duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Meets other continuation criteria as described in Section A above

2. Individual's condition responded while on therapy
   - Response is defined as AT LEAST a 20% improvement in the signs and symptoms of Crohn's disease

   Renewal Duration: 12 months

Section F. Moderately to severely active Ulcerative Colitis (UC):

- **Criteria for initial therapy:** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met for moderately to severely active ulcerative colitis (UC):

1. Request is for **ONE** of the following: Humira, Simponi (not Simponi Aria), Xeljanz IR

2. Prescriber is a Gastroenterologist

3. Meets other initial criteria per indication or use as described in Section A above

4. Individual is 18 years of age and older

BIOLOGIC AND IMMUNOLOGICAL AGENTS (cont.)

5. Diagnosis of moderate to severe active ulcerative colitis, as indicated by **ONE or more** of the following:
   - Anemia
   - Bowel movements 4 or more times per day
   - Fever
   - Nocturnal stools
   - Persistent abdominal pain
   - Tachycardia
   - Visible blood in stool

6. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **ONE or more** of the following:
   - 6-mercaptopurine
   - Azathioprine
   - Oral corticosteroids
   - Salicylates

7. For **non-preferred agents** for ulcerative colitis (UC):
   Xeljanz IR
   - Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **TWO** of the following preferred agents:
     - Humira
     - Simponi

   Approval Duration: 6 months

➢ **Criteria for continuation of coverage (renewal request):** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Meets other continuation criteria as described in Section A above

2. Individual's condition responded while on therapy
   - Response is defined as AT LEAST a 20% improvement in signs and symptoms of ulcerative colitis

   Renewal Duration: 12 months

Section G. Polyarticular Juvenile Idiopathic Arthritis (pJIA):

➢ **Criteria for initial therapy:** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met for polyarticular juvenile idiopathic arthritis:

1. Request is for **ONE** of the following: Enbrel, Humira, Orencia (IV&SQ)

2. Prescriber is a Rheumatologist

3. Meets other initial criteria per indication or use as described in Section A above

4. Individual is 2 years of age and older

5. Treatment needed for disease severity, as indicated by **ONE or more** of the following:
   - Four or fewer joints involved and inadequate response to **ALL** of the following:
     - Glucocorticosteroid injection or NSAIDs
     - Methotrexate
   - Five or more joints involved and intolerance of or inadequate response to methotrexate
   - Sacroiliitis, and intolerance of or inadequate response to methotrexate
   - Uveitis, and inadequate response to **ALL** of the following:
     - Systemic corticosteroids
     - Systemic immunosuppressant (eg, azathioprine or methotrexate)
     - Topical ophthalmic corticosteroids

6. For **non-preferred agents** for polyarticular juvenile idiopathic arthritis:
   Enbrel, Orencia (IV&SQ):
   - Individual has failure (used for $\geq$ 3 consecutive months), contraindication or intolerance to Humira

   Approval Duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Meets other continuation criteria as described in Section A above

2. Individual's condition responded while on therapy
   - Response is defined as AT LEAST a 30% improvement in JIA Core Set (see Definition section)

   Renewal Duration: 12 months

Section H. Moderate to severe chronic Plaque Psoriasis (PP):

- **Criteria for initial therapy:** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met for moderate to severe chronic plaque psoriasis:

1. Request is for **ONE** of the following: Cimzia, Cosentyx, Enbrel, Humira, Otezla, Stelara, Siliq, Taltz, Tremfya

2. Prescriber is a Dermatologist

3. Meets other initial criteria per indication or use as described in Section A above

4. Individual is 18 years of age and older

5. Diagnosis of moderate to severe plaque psoriasis, as indicated by **ALL** of the following:
   - Body surface area involvement of 10% or more
   - Candidate for systemic therapy or phototherapy

BIOLOGIC AND IMMUNOLOGICAL AGENTS (cont.)

6. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to other treatments to control psoriasis as indicated by **TWO or more** of the following:
   - Immunosuppressive treatments (e.g., cyclosporine, methotrexate)
   - Photochemotherapy (i.e., psoralen plus ultraviolet A therapy)
   - Phototherapy (i.e., ultraviolet light therapy)
   - Topical agents (e.g., anthralin, calcipotriene, coal tars, corticosteroids, tazarotene)
   - Tumor necrosis factor-alpha inhibitor

7. No concomitant systemic therapy or phototherapy

8. For **non-preferred agents** for plaque psoriasis:

   Cosentyx:
   - Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **ONE** of the following preferred agents:
     - Humira
     - Otezla
     - Stelara
     - Tremfya

   Enbrel, Siliq, Taltz:
   - **ALL** of the following:
     - Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **ONE** of the following preferred agents:
       - Humira
       - Otezla
       - Stelara
       - Tremfya
     - Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to:
       - Cosentyx

   Approval Duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Meets other continuation criteria as described in Section A above

2. Individual's condition responded while on therapy
   - Response is defined as AT LEAST a 20% improvement in PASI (see Definition section)

   Renewal Duration: 12 months

BIOLOGIC AND IMMUNOLOGICAL AGENTS (cont.)

Section I. Moderate to severe Hidradenitis Suppurativa:

- **Criteria for initial therapy:** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met for moderate to severe hidradenitis suppurativa:

  1. Request is for Humira
  2. Prescriber is a Dermatologist
  3. Meets other initial criteria per indication or use as described in Section A above
  4. Individual is 18 years of age and older
  5. Diagnosis of moderate to severe disease as indicated by **ONE or more** of the following:
     - Multiple interconnected tracts and abscesses in single anatomic area
     - Widely separated and recurrent abscesses with sinus tracts and scarring
  6. Individual has failure, contraindication or intolerance to oral antibiotics (at maximum recommended doses) for at least 3 consecutive months (i.e. clindamycin, minocycline, doxycycline, rifampin)

  Approval Duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Meets other continuation criteria as described in Section A above
  2. Individual's condition responded while on therapy
     - Response is defined as AT LEAST a 20% improvement in the signs and symptoms of hidradenitis suppurativa

  Renewal Duration: 12 months

Section J. Moderate Non-infectious Intermittent Uveitis, Non-infectious posterior Uveitis, or Non-infectious Panuveitis:

- **Criteria for initial therapy:** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met for moderate non-infectious intermediate uveitis, non-infectious posterior uveitis or non-infectious panuveitis:

  1. Request is for Humira
  2. Prescriber is an Ophthalmologist
  3. Meets other initial criteria per indication or use as described in Section A above

4. Individual is 18 years of age and older

5. Individual has failure, contraindication or intolerance to **ONE** agent for both categories:
    - Corticosteroids (> 2 week trial at up to maximally indicated doses)
    - Systemic immunosuppressant (i.e. methotrexate, cyclosporine, azathioprine, mycophenolate, cyclophosphamide, leflunomide, hydroxychloroquine, sulfasalazine, tacromilus, sirolimus, or chlorambucil)

Approval Duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Meets other continuation criteria as described in Section A above

2. Individual's condition responded while on therapy
    - Response is defined as AT LEAST a 20% improvement in the signs and symptoms of uveitis or panuveiitis

Renewal Duration: 12 months

Section K. Moderate Non-infectious Uveitis refractory to corticosteroids:

- **Criteria for initial therapy:** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met for non-infectious uveitis refractory to a systemic corticosteroid:

1. Request is for Humira

2. Prescriber is an Ophthalmologist

3. Meets other initial criteria per indication or use as described in Section A above

4. Age 4 through 17 years

5. Individual has failure, contraindication or intolerance to use of a systemic immunosuppressant (e.g., methotrexate, cyclosporine, azathioprine, mycophenolate, cyclophosphamide, leflunomide, hydroxychloroquine, sulfasalazine, tacromilus, sirolimus, or chlorambucil)

Approval Duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Meets other continuation criteria as described in Section A above

BIOLOGIC AND IMMUNOLOGICAL AGENTS (cont.)

2. Individual's condition responded while on therapy
   - Response is defined as AT LEAST 20% improvement in signs and symptoms of uveitis

   Renewal Duration: 12 months

Section L. Moderate Giant Cell Arteritis:

- **Criteria for initial therapy:** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met for moderate giant cell arteritis:

1. Request is for Actemra
2. Prescriber is a Rheumatologist
3. Meets other initial criteria per indication or use as described in Section A above
4. Individual is 18 years of age or older
5. Diagnosis is confirmed by Temporal artery biopsy
6. Individual has failure (used for $\geq$ 3 consecutive months), contraindication or intolerance to **glucocorticoids**

   Approval Duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Meets other continuation criteria as described in Section A above
2. Individual's condition responded while on therapy
   - Response is defined as AT LEAST 20% improvement in signs and symptoms of giant cell arteritis

   Renewal duration: 12 months

Section M. Cytokine Release Syndrome:

- **Criteria for initial therapy:** Biologic and Immunological Agents is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met for chimeric antigen receptor (CAR) T cell–induced severe or life-threatening cytokine release syndrome:

1. Request is for Actemra
2. No evidence of active infection, including any localized infections

BIOLOGIC AND IMMUNOLOGICAL AGENTS (cont.)

3. Individual has been previously evaluated for tuberculosis risk factors and tested for latent infection and treatment with standard anti-mycobacterial medication(s) is initiated, if indicated, prior to the initiation of Actemra.

4. No active hepatic disease or hepatic impairment

5. ALT (alanine aminotransferase) or AST (aspartate aminotransferase) is $\leq$ 1.5 times the upper limit of normal

6. Absolute neutrophil count (ANC) is equal to or greater than 2,000/mm^3

7. Platelet count is equal to or greater than 100,000/mm^3

8. Live vaccines will not be given concurrently with Actemra

9. No concurrent treatment with any other biological DMARDs such as TNF antagonists, IL-1R (interleukin 1) antagonists, anti-CD-20 monoclonal antibodies or co-stimulation modulators

   Approval Duration: One time only

Section N. Measurement of Antibodies to Biologic/Immunologic Agents:

- Measurement of antibodies for biologic or immunologic agents in an individual receiving treatment, either alone or as a combination test, which includes the measurement of serum levels for the biologic or immunologic agents is considered ***experimental or investigational*** based upon:

  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  2. Insufficient evidence to support improvement of the net health outcome.

  These measurements include, *but are not limited to:*
  - Anser™ ADA

- **Biologic and Immunological Agents therapy for all other indications not previously listed** is considered ***experimental or investigational*** based upon:

  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  5. Insufficient evidence to support improvement outside the investigational setting.

  These indications include, *but are not limited to:*
  - Treatment with dosing or frequency outside the FDA-approved dosing and frequency

BIOLOGIC AND IMMUNOLOGICAL AGENTS (cont.)

Definitions:

Adult: Age 18 years and older.

Uveitis:
Uveitis is characterized by inflammation of the uvea, which is the middle portion of the eye made up of the iris, ciliary body and choroid. The anterior portion of the uvea includes the iris and ciliary body, the posterior portion of the uvea is known as the choroid. There are several types of uveitis, defined by the part of the eye where it occurs:

- Iritis also called anterior uveitis, is the most common type of uveitis
- Intermediate uveitis or pars planitis is inflammation of the uvea in the middle or intermediate region of the eye
- Posterior uveitis affects the back parts of your eye
- Panuveitis occurs when all layers of the uvea are inflamed

Preferred and Non-preferred Agents:

Disease State	Preferred Agents	Non-Preferred Agents
Rheumatoid Arthritis (RA)	Cimzia Humira Simponi Simponi Aria	Actemra QSE Enbrel QSE Kevzara DSE Kineret QSE Orencia (IV&SQ) QSE Rituxan QSE Xeljanz IR, Xeljanz XR DSE
Psoriatic Arthritis (PsA)	Cimzia Humira Otezla Simponi Simponi Aria Stelara	Cosentyx DSE Enbrel QSE Orencia (IV&SQ) QSE Taltz QSE Xeljanz IR, Xeljanz XR DSE
Psoriasis (PsO)	Humira Otezla Stelara Tremfya	Enbrel DSE Siliq DSE Taltz DSE Cosentyx –single step
Ankylosing Spondylitis	Cimzia Humira Simponi Simponi Aria	Cosentyx DSE Enbrel DSE
All other indications		DSE through two preferred agents
DSE: Double Step Edit. Individual has failure, contraindication or intolerance to at least **two** preferred agents with a specific duration. QSE: Quadruple Step Edit. Individual has failure, contraindication or intolerance to at least **four** preferred agents with a specific duration.		

BIOLOGIC AND IMMUNOLOGICAL AGENTS (cont.)

Rheumatoid Arthritis Disease Activity Measurement Instruments:

Instrument	Threshold of Disease Activity
Clinical Disease Activity Index (CDAI)	Range: 0 to 76 Remission: ≤ 2.8 Low activity: >2.8 to ≤ 10 Moderate activity: >10 to ≤ 22 High activity: >22
Disease Activity Score 28 (DAS28)	Range: 0.5 to 9 Remission: < 2.6 Low activity: > 2.6 to ≤ 3.2 Moderate activity: > 3.2 to ≤ 5.1 High activity: > 5.1
Patient Activity Scale (PAS) Patient Activity Scale II (PASII)	Range 0 to 10 Remission: 0 to 0.25 Low activity: >0.25 to 3.7 Moderate activity: > 3.7 to < 8.0 High activity: ≥ 8.0
Routine Assessment of Patient Index Data 3 (RAPID-3)	Range: 0 to 10 Remission: 0 to 1.0 Low activity: > 1.0 to 2.0 Moderate activity: > 2.0 to 4.0 High activity: > 4.0 to 10
Simplified Disease Activity Index (SDAI)	Range: 0 to 90 Remission: ≤ 3.3 Low activity: > 3.3 to ≤ 11.0 Moderate activity: > 11.0 to ≤ 26 High activity: > 26

American College of Rheumatology 20 Percent Improvement Criteria (ACR20):

At least 20 percent improvement in the following:
1. Swollen joint count
2. Tender joint count
And three of the following five variables:
3. Patient-assessed global disease activity (e.g., by VAS)
4. Evaluator-assessed global disease activity (e.g., by VAS)
5. Patient pain assessment (e.g., by VAS)
6. Functional disability (e.g., by HAQ)
7. Acute phase response (ESR or CRP)
A 50 and 70 percent ACR response (ACR50 and ACR70, respectively) represents respective improvement of at least 50 or 70 percent[1].
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BIOLOGIC AND IMMUNOLOGICAL AGENTS (cont.)

1. *Felson DT, Anderson JJ, Lange ML, et al. Should improvement in rheumatoid arthritis clinical trials be defined as fifty percent or seventy percent improvement in core set measures, rather than twenty percent?. Arthritis Rheum 1998; 41:1564.*
2. *Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. Arthritis Rheum 1995; 38:727.*

JIA Core Set 30%

At least 30 percent improvement in at least 3 of the 6 core set variables with no more than 1 remaining variable worsening by > 30%
1. Physician's global assessment of overall disease activity measured on a visual analog scale (VAS)
2. Parent or patient global assessment of overall well-being measured on VAS
3. Functional ability
4. Number of joints with active arthritis
5. Number of joints with limited range of motion
6. Erythrocyte sedimentation rate (ESR)
Giannini, EH, Ruperto, N, Ravelli A, et al. Preliminary Definition of Improvement in Juvenile Arthritis. Arthritis & Rheumatism 1997

Bath Ankylosing Spondylitis Disease Activity Index (BASDAI):

1. How would you describe the overall level of fatigue/tiredness you have experienced?			
	None	0 1 2 3 4 5 6 7 8 9 10	Very Severe
2. How would you describe the overall level of ankylosing spondylitis **neck, back or hip pain** you have had?			
	None	0 1 2 3 4 5 6 7 8 9 10	Very Severe
3. How would you describe the overall level of pain/swelling you have had in joints other than neck, back and hips?			
	None	0 1 2 3 4 5 6 7 8 9 10	Very Severe
4. How would you describe the level of discomfort you have had from an area tender to touch or pressure?			
	None	0 1 2 3 4 5 6 7 8 9 10	Very Severe
5. How would you describe the level of morning stiffness you have had from the time you wake up?			
	None	0 1 2 3 4 5 6 7 8 9 10	Very Severe
6. How long does your morning stiffness last from the time you wake up?			
	0 hours	0 1 2 3 4 5 6 7 8 9 10	2 or more hours

Calculation of BASDAI:
Compute the mean of questions 5 and 6
Calculate the sum of the values of question 1-4 and add the result to the mean of questions 5 and 6

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Originally published in: Garrett S, Jenkinson T, Kennedy LG, et al. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol 1994; 21:2286. Reproduced with permission from: the Royal National Hospital for Rheumatic Diseases NHS Foundation Trust, Bath. www.rnhrd.nhs.uk. Copyright ©

BIOLOGIC AND IMMUNOLOGICAL AGENTS (cont.)

Psoriasis Area and Severity Index (PASI):

	Head	Upper Extremities	Trunk	Lower extremities
1. Redness[1]				
2. Thickness[1]				
3. Scale[1]				
4. Sum of rows 1,2 and 3				
5. Area score[2]				
6. Score of row 4 x row 5 x the area multiplier	row 4 x row 5 x 0.1	row 4 x row 5 x 0.2	Row 4 x row 5 x 0.3	Row 4 x row 5 x 0.4
7. Sum row 6 for each column for PASI score				

Steps in generating PASI score

(a) Divide body into four areas: head, arms, trunk to groin, and legs to top of buttocks.
(b) Generate an average score for the erythema, thickness, and scale for each of the 4 areas (0 = clear; 1–4 = increasing severity)[1].
(c) Sum scores of erythema, thickness, and scale for each area.
(d) Generate a percentage for skin covered with psoriasis for each area and convert that to a 0–6 scale (0 = 0%; 1 = <10%; 2 = 10–<30%; 3 = 30–<50%; 4 = 50–<70%; 5 = 70–<90%; 6 = 90–100%).
(e) Multiply score of item (c) above times item (d) above for each area and multiply that by 0.1, 0.2, 0.3, and 0.4 for head, arms, trunk, and legs, respectively.
(f) Add these scores to get the PASI score.

[1] Erythema, induration and scale are measured on a 0–4 scale (none, slight, mild, moderate, severe)
[2] Area scoring criteria (score: % involvement)
0: 0 (clear)
1: <10%
2: 10–<30%
3: 30–<50%
4: 50–<70%
5: 70–<90%
6: 90–<100%

Feldman, SR and Krueger, GG. Psoriasis assessment tools in clinical trials. Ann Rheum Dis 2005; 64 (Suppl III): ii65-ii68.

Resources:

1. 2.04.84 BCBS Association Medical Policy Reference Manual. Measurement of Serum Antibodies to Infliximab and Adalimumab. Re-issue date 11/09/2017, issue date 08/09/2012.

2. 5.01.24 BCBS Association Medical Policy Reference Manual. Nononcologic Uses of Rituximab. Re-issue date 10/12/2017, issue date 10/09/2014.

3. American Academy of Ophthalmology. What is Uveitis? 03/10/2014.

4. Bartelds GM, Krieckaert CL, Nurmohamed MT, et al. Development of antidrug antibodies against adalimumab and association with disease activity and treatment failure during long-term follow-up. *JAMA.* Apr 13 2011;305(14):1460-1468.

5. Foeldvari I, Nielsen S, Kummerle-Deschner J, et al. Tumor necrosis factor-alpha blocker in treatment of juvenile idiopathic arthritis-associated uveitis refractory to second-line agents: results of a multinational survey. *J Rheumatol.* 2007 May 2007;34(5):1146-1150.

6. Magli A, Forte R, Navarro P, et al. Adalimumab for juvenile idiopathic arthritis-associated uveitis. *Graefes Arch Clin Exp Ophthalmol.* Jun 2013;251(6):1601-1606.

7. Rifkin LM, Birnbaum AD, Goldstein DA. TNF Inhibition for Ophthalmic Indications: Current Status and Outlook. *BioDrugs.* Aug 2013;27(4):347-357.

8. Sen ES, Sharma S, Hinchcliffe A, Dick AD, Ramanan AV. Use of adalimumab in refractory non-infectious childhood chronic uveitis: efficacy in ocular disease--a case cohort interventional study. *Rheumatology (Oxford).* Dec 2012;51(12):2199-2203.

9. Simonini G, Taddio A, Cattalini M, et al. Prevention of flare recurrences in childhood-refractory chronic uveitis: an open-label comparative study of adalimumab versus infliximab. *Arthritis Care Res (Hoboken).* Apr 2011;63(4):612-618.

10. Suhler EB, Lowder CY, Goldstein DA, et al. Adalimumab therapy for refractory uveitis: results of a multicentre, open-label, prospective trial. *Br J Ophthalmol.* Apr 2013;97(4):481-486.

11. UpToDate.com. Uveitis: Etiology, clinical manifestations, and diagnosis. 02/24/2017.

12. Vazquez-Cobian LB, Flynn T, Lehman TJ. Adalimumab therapy for childhood uveitis. *J Pediatr.* Oct 2006;149(4):572-575.

Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:		Office Fax:

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:		Dosage Form:
Directions for Use:	Quantity:	Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: ________________________________ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. What is the diagnosis? Please specify below.

ICD-10 Code: ____________________ **Diagnosis Description:** ______________________________

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. What medication(s) has the individual tried and failed for this diagnosis? Please specify below.
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. Are there any supporting labs or test results? Please specify below.

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature:	Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.