BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 4/01/2019
LAST REVIEW DATE: 11/19/2020
LAST CRITERIA REVISION DATE: 11/19/2020
ARCHIVE DATE:

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
OLUMIANT® (baricitinib) oral tablet
ORENCIA® (abatacept) intravenous and subcutaneous injection (IV&SQ)
OTEZLA® (apremilast) oral tablet
RINVOQ™ (upadactinib) extended release tablet
SILIQ™ (brodalumab) subcutaneous injection
SIMPONI® (golimumab) subcutaneous injection
SIMPONI ARIA® (golimumab) intravenous solution
SKYRIZI™ (risankizumab-rzaa) subcutaneous injection
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.

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BIOLOGIC AND IMMUNOLOGICAL AGENTS

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

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-M below

  3. Serologic tests for hepatitis B and C (HB surface Ag, anti-HB surface Ab, anti-HB core Ab, and hepatitis C antibody tests) have been done within the previous 12 months **(Does not apply for Otezla)**

  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. Individual does not have untreated Chronic or Acute Hepatitis B or C **(Does not apply for Otezla)**

7. There is no concurrent use of live vaccines **(Does not apply for Otezla)**
8. There is no concurrent use with other biologic and immunologic agents
9. Requested medication is prescribed in accordance with the prescribing information and does not have any significant interacting drugs and/or disease states (i.e. abnormal labs)

- **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-M 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. 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)**
6. Individual does not have untreated latent or active tuberculosis **(Does not apply for Otezla)**
7. Individual does not have untreated Chronic or Acute Hepatitis B or C **(Does not apply for Otezla)**
8. There is no concurrent use of live vaccines **(Does not apply for Otezla)**
9. Concomitant disease states have been evaluated for risk potential and symptoms will be monitored
10. There is no concurrent use with other biologic and immunologic agents
11. 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, Olumiant, Orencia (IV&SQ), Rinvoq, 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. Age of individual is consistent with the FDA approved product labeling

5. Diagnosis of rheumatoid arthritis identified by **ONE** of the following:
    a. Clinical Disease Activity Index (CDAI) score greater than 10
    b. Disease Activity Score 28 (DAS28) of greater than 3.2
    c. Patient Activity Scale (PAS) of greater than 3.7
    d. Patient Activity Scale II (PASII) of greater than 3.7
    e. Routine Assessment of Patient Index Data 3 (RAPID-3) score greater than 2
    f. Simplified Disease Activity Index (SDAI) score greater than 11

6. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **methotrexate**

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

8. For **non-preferred agents** for rheumatoid arthritis:
    Actemra, Orencia (IV&SQ):
    a. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **TWO** of the following preferred agents:
        i. Cimzia
        ii. Humira
        iii. Rinvoq
        iv. Simponi or Simponi Aria
        v. Xeljanz IR or Xeljanz XR

    Enbrel, Kevzara, Kineret, Olumiant:
    b. **ALL** of the following:
        i. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **TWO** of the following preferred agents:
            1. Cimzia
            2. Humira
            3. Rinvoq
            4. Simponi or Simponi Aria
            5. Xeljanz IR or Xeljanz XR

        ii. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **BOTH** of the following:
            1. Actemra
            2. Orencia (IV&SQ)

Approval Duration: 6 months

- **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
     a. 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 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, Simponi Aria, Stelara, Taltz, Tremfya, 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. Age of individual is consistent with the FDA approved product labeling

  5. Diagnosis of moderate to severe active psoriatic arthritis is identified by **ONE or more** of the following:
     a. Predominantly axial disease (i.e. sacroiliitis or spondylitis) as indicated by **ALL** of the following:
        i. Radiographic evidence of axial disease (e.g., sacroiliac joint space narrowing or erosions, vertebral syndesmophytes)
        ii. Symptoms (e.g., limited spinal range of motion, spinal morning stiffness more than 30 minutes) present for more than 3 months' duration
        iii. Failure or intolerance of 1 or more different NSAIDs (at maximum recommended doses) over total period of at least 4 or more weeks of therapy
     b. Predominantly non-axial disease, and failure (used for ≥ 3 consecutive months), intolerance, or contraindication to methotrexate or NSAIDs

  6. For **non-preferred agents** for psoriatic arthritis:
     Taltz:
     a. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **ONE** of the following preferred agents:
        i. Cimzia

ii. Humira
iii. Simponi and Simponi Aria
iv. Stelara
v. Tremfya

Orencia (IV&SQ), Xeljanz IR, Xeljanz XR:

a. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **TWO** of the following preferred agents:
   i. Cimzia
   ii. Humira
   iii. Simponi and Simponi Aria
   iv. Stelara
   v. Tremfya

Cosentyx:

a. **ALL** of the following:
   i. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **TWO** of the following preferred agents:
      1. Cimzia
      2. Humira
      3. Simponi or Simponi Aria
      4. Stelara
      5. Tremfya

   ii. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **BOTH** of the following:
      1. Taltz
      2. Orencia (IV&SQ) or Xeljanz IR or Xeljanz XR

Enbrel:

a. **ALL** of the following:
   i. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **TWO** of the following preferred agents:
      1. Cimzia
      2. Humira
      3. Simponi or Simponi Aria
      4. Stelara
      5. Tremfya
   ii. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **Two** of the following:
      1. Taltz
      2. Orencia (IV&SQ)
      3. Xeljanz IR or Xeljanz XR

Approval Duration: 6 months

BIOLOGIC AND IMMUNOLOGICAL AGENTS

- **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
     a. 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, Taltz

  2. Prescriber is a Rheumatologist

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

  4. Age of individual is consistent with the FDA approved product labeling

  5. Clinical and diagnostic imaging evidence of ankylosing spondylitis as indicated by **ALL** of the following:
     a. Back pain of 3 months or more duration and age of onset of 45 years or younger
     b. Sacroiliitis on imaging
     c. Spondyloarthritis signs or symptoms as indicated by **ONE or more** of the following:
        i. Arthritis
        ii. Elevated serum C-reactive protein
        iii. Enthesitis (e.g., inflammation of Achilles tendon insertion)
        iv. HLA-B27
        v. Limited chest expansion
        vi. Morning stiffness for one hour or more

  6. Disease activity and treatment scenario as indicated by **ONE or more** of the following:
     a. Axial (spinal) disease
     b. Failure of or intolerance to treatment with anti-tumor necrosis factor-alpha drug
     c. 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:
   Taltz:
   a. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **ONE** of the following preferred agents:
      i. Cimzia
      ii. Humira
      iii. Simponi or Simponi Aria

   Cosentyx, Enbrel:
   b. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **TWO** of the following preferred agents:
      i. Cimzia
      ii. Humira
      iii. Simponi or Simponi Aria

   c. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to the following:
      i. Taltz

   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
   a. 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 is consistent with the FDA approved product labeling

5. Diagnosis of moderate to severe active Crohn disease as indicated by **ONE or more** of the following:
    a. Abdominal abscess
    b. Anemia
    c. Dehydration
    d. Elevated serum C-reactive protein level
    e. Fever
    f. Intermittent vomiting
    g. Intestinal obstruction
    h. 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:
    a. 6-mercaptopurine
    b. Azathioprine
    c. Methotrexate
    d. 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
    a. 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), Stelara, Xeljanz IR

2. Prescriber is a Gastroenterologist

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

4. Age of individual is consistent with the FDA approved product labeling

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

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

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

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
    a. 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: Actemra, Enbrel, Humira, Orencia (IV&SQ), Xeljanz

2. Prescriber is a Rheumatologist

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

4. Age of individual is consistent with the FDA approved product labeling

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

6. For **Xeljanz:**
    a. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to Humira.

7. For **non-preferred agents** for polyarticular juvenile idiopathic arthritis:
    Actemra, Orencia (IV&SQ):
    a. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to Humira

    Enbrel:
    a. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to the following preferred agent:
        ii. Humira

    b. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **ALL** of the following:
        iii. Actemra
        iv. Orencia (IV&SQ)

    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
    a. 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, Skyrizi, Taltz, Tremfya

2. Prescriber is a Dermatologist

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

4. Age of individual is consistent with the FDA approved product labeling

5. Diagnosis of moderate to severe plaque psoriasis, as indicated by **ALL** of the following:
   a. Is a candidate for photochemotherapy or phototherapy
   b. Plaque psoriasis involves ≥ 10% body surface area (BSA) **or** plaque psoriasis involves < 10% BSA but includes sensitive areas or areas that significantly impact daily function (e.g. palms, soles of feet, head/neck, or genitalia)
   c. A Psoriasis Area and Index (PASI) of at least 10

6. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to a treatment regimen that includes **ALL** of the following:
   a. A trial of least **TWO** topical agents (e.g., anthralin, calcipotriene, coal tars, corticosteroids, tazarotene)
   b. A trial of **ONE** immunosuppressive treatment (e.g., cyclosporine, methotrexate)
   c. A trial of Ultraviolet Light therapy (e.g., Photochemotherapy (i.e., psoralen plus ultraviolet A therapy), Phototherapy (i.e., ultraviolet light therapy), or Excimer laser)

7. No concomitant systemic therapy or phototherapy

8. For **non-preferred agents** for plaque psoriasis:
   Taltz:
   a. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **ONE** of the following preferred agents:
      i. Cimzia
      ii. Humira
      iii. Skyrizi
      iv. Stelara
      v. Tremfya

Cosentyx, Enbrel, Siliq:

a. **ALL** of the following:
   i. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **THREE** of the following preferred agents:
      1. Cimzia
      2. Humira
      3. Skyrizi
      4. Stelara
      5. Tremfya

   ii. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to:
      1. Taltz

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
   a. Response is defined as AT LEAST a 20% improvement in PASI (see Definition section)

Renewal Duration: 12 months

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. Age of individual is consistent with the FDA approved product labeling

5. Diagnosis of moderate to severe disease as indicated by **ONE or more** of the following:
   a. Multiple interconnected tracts and abscesses in single anatomic area
   b. 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
   a. 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. Age of individual is consistent with the FDA approved product labeling

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

Approval Duration: 6 months

BIOLOGIC AND IMMUNOLOGICAL AGENTS

- **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
     a. Response is defined as AT LEAST a 20% improvement in the signs and symptoms of uveitis or panuveitis

  Renewal Duration: 12 months

Section K. 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. Age of individual is consistent with the FDA approved product labeling

  5. Diagnosis is confirmed by temporal artery biopsy

  6. Individual has failure (used for ≥ 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
     a. Response is defined as AT LEAST 20% improvement in signs and symptoms of giant cell arteritis

  Renewal duration: 12 months

BIOLOGIC AND IMMUNOLOGICAL AGENTS

Section L. 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 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 M. Behcet's Disease:

- **Criteria for initial therapy:** Otezla is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met for oral ulcers associated with Behcet's Disease

  1. Request is for Otezla

  2. Prescriber is or in consultation with a Rheumatologist
  3. Meets other initial criteria per indication or use as described in Section A above

  4. Age of individual is consistent with the FDA approved product labeling

  5. Diagnosis is confirmed by meeting International Study Group (ISG) criteria for Behcet's Disease (see Definitions section) with **ALL** of the following:
     a. Two or more active oral ulcer without major organ involvement
     b. Oral ulcers that occurred 3 or more times in previous 12 months
     c. Does not require systemic immunosuppressants (e.g. biologics, corticosteroids, azathioprine)
     d. No concurrent therapy with topical corticosteroids

  6. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to **TWO** of the following:
     a. Oral or topical corticosteroids
     b. Nonsteroidal anti-inflammatory drugs (NSAIDs)
     c. Colchicine
     d. Immunosuppressant

     Approval Duration: 6 months

BIOLOGIC AND IMMUNOLOGICAL AGENTS

- **Criteria for continuation of coverage (renewal request):** Otezla 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
     a. Response is defined as AT LEAST 20% improvement in signs and symptoms of oral ulcers

  Renewal duration: 12 months

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

Definitions:

Preferred and Non-Preferred Agents:

Disease State	Preferred Agents	Non-Preferred Agents
Rheumatoid Arthritis (RA)	Cimzia Humira Rinvoq Simponi Simponi Aria Xeljanz IR Xeljanz XR	Actemra DSE Enbrel QSE Kevzara QSE Kineret QSE Olumiant QSE Orencia (IV&SQ) DSE
Psoriatic Arthritis (PsA)	Cimzia Humira Otezla Simponi Simponi Aria Stelara	Cosentyx QSE Enbrel QSE Orencia (IV&SQ) DSE Taltz SSE Xeljanz IR, Xeljanz XR DSE
Psoriasis (PsO)	Cimzia Humira Otezla Skyrizi Stelara Tremfya	Cosentyx QSE Enbrel QSE Siliq QSE Taltz SSE
Ankylosing Spondylitis	Cimzia Humira Simponi Simponi Aria	Cosentyx TSE Enbrel TSE Taltz SSE
Juvenile Idiopathic Arthritis	Humira	Actemra SSE Enbrel TSE Orencia SSE
All other indications		DSE through two preferred agents

SSE: Single Step Edit. Individual has failure, contraindication or intolerance to at least **one** preferred agent with a specific duration.
DSE: Double Step Edit. Individual has failure, contraindication or intolerance to at least **two** preferred agents with a specific duration.
TSE: Triple Step Edit. Individual has failure, contraindication or intolerance to at least **three** 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.

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

BIOLOGIC AND IMMUNOLOGICAL AGENTS

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].
 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.*

BIOLOGIC AND IMMUNOLOGICAL AGENTS

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

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				

BIOLOGIC AND IMMUNOLOGICAL AGENTS

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.

Diagnostic criteria for Behçet's syndrome:

Criterion	Required features
Recurrent oral ulceration	Aphthous (idiopathic) ulceration, observed by clinician or patient, with at least three episodes in any 12-month period
Plus any two of the following:	
Recurrent genital ulceration	Aphthous ulceration or scarring, observed by clinician or patient
Eye lesions	Anterior or posterior uveitis cells in vitreous in slit-lamp examination; or retinal vasculitis documented by ophthalmologist
Skin lesions	Erythema nodosum-like lesions observed by clinician or patient; papulopustular skin lesions or pseudofolliculitis with characteristic acneiform nodules observed by clinician
Pathergy test	Interpreted at 24 to 48 hours by clinician

Adapted from International Study Group for Behcet's Disease. Criteria for diagnosis of Behcet's disease. Lancet 1990; 335:1078.

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.

13. UpToDate.com: Clinical manifestations and diagnosis of Behçet syndrome. 11/20/2019.