BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 4/01/2019**
SECTION: DRUGS	**LAST REVIEW DATE: 2/17/2022**
	LAST CRITERIA REVISION DATE: 2/17/2022
	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, oral solution
XELJANZ® XR (tofacitinib citrate) oral 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.

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.**

Criteria:

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

  3. Meets other additional initial criteria per indication or use as described below in Sections B-O below

4. 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)**
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. There are **NO** FDA-label contraindications
10. There is no concurrent use with other biologic and immunologic agents
11. 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 additional continuation criteria per indication or use as described in Sections B-P below
3. Individual has been adherent with the medication
4. Individual has not developed any contraindications per FDA label or other significant adverse drug effects that may exclude continued use
5. Individual does not have untreated Chronic or Acute Hepatitis B or C **(Does not apply for Otezla)**
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. 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 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, Xeljanz tab, Xeljanz XR, Taltz

2. Prescriber is a Rheumatologist

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

4. 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

5. Disease activity and treatment scenario as indicated by **ONE or more** of the following:
    a. Axial (spinal) disease
    b. Peripheral arthritis without axial involvement, and failure, contraindication per FDA label, or intolerance of 4 or more months of therapy with sulfasalazine

6. Individual has failure, contraindication per FDA label, 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

7. For **non-preferred agents** for ankylosing spondylitis:
    Taltz:
    a. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **ONE** of the following preferred agents:
        i. Cimzia
        ii. Humira
        iii. Simponi or Simponi Aria

    Xeljanz tab, Xeljanz XR:
    a. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **TWO** of the following preferred agents:

i. Cimzia
ii. Humira
iii. Simponi or Simponi Aria

Enbrel:
a. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **TWO** of the following preferred agents:
   i. Cimzia
   ii. Humira
   iii. Simponi or Simponi Aria
b. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **ONE** of the following:
   i. Taltz
   ii. Xeljanz tab or Xeljanz XR

Cosentyx:
a. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **TWO** of the following preferred agents:
   i. Cimzia
   ii. Humira
   iii. Simponi or Simponi Aria
b. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, 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. **With first request for continuation**: Response is defined as AT LEAST a 20% improvement in BASDAI (see Definition section)
   b. **With subsequent request for continuation**: Documented evidence of disease stability and/or improvement with no evidence of disease progression

Renewal Duration: 12 months

Section C. 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. A confirmed diagnosis of moderate to severe active Crohn's disease as indicated by **ONE** of the following:
     a. Crohn's disease activity index (CDAI) greater than 220 in adults
     b. Pediatric Crohn's disease activity index (PCDAI) greater than 30
     c. **At least 5** of the following signs and symptoms:
        i. Anemia
        ii. Chronic intermittent diarrhea (with or without food)
        iii. Crampy abdominal pain
        iv. Elevated serum C-reactive protein level and/or fecal calprotectin
        v. Extraintestinal manifestations such as arthritis or arthropathy, eye and skin disorders, biliary tract involvement, and kidney stones
        vi. Fatigue
        vii. Fistulas
        viii. Perianal disease (e.g., anal fissures, anorectal abscess)
        ix. Weight loss or growth failure in children

  5. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **ONE or more** of the following [Note this criterion is waived if the individual already has tried an FDA-approved Crohn's disease biologic]:
     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. **With first request for continuation ONE of the following:**

i. AT LEAST a 20% improvement in the signs and symptoms of Crohn's disease
ii. Decrease in Crohn's disease activity index of more than 70 from baseline or a Crohn's disease activity index of < 150 (in remission) in adults
iii. Pediatric Crohn disease activity index (PCDAI) ≤ 30 in children indicating mild disease or disease remission

b. **With subsequent request for continuation**: Documented evidence of disease stability and/or improvement with no evidence of disease progression

Renewal Duration: 12 months

Section D. 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, Siliq, Skyrizi, Stelara, Taltz, Tremfya

2. Prescriber is a Dermatologist

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

4. 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

5. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, 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)

6. No concomitant use of other systemic therapy

7. For **non-preferred agents** for plaque psoriasis:
   Taltz:
   a. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, 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 per FDA label, 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 per FDA label, 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. **With first request for continuation:** Response is defined as AT LEAST a 20% improvement in PASI (see Definition section)
   b. **With subsequent request for continuation**: Documented evidence of disease stability and/or improvement with no evidence of disease progression

Renewal Duration: 12 months

Section E. 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 **(IV&SQ)**, Enbrel, Humira, Orencia (IV&SQ), Simponi Aria, Xeljanz tab, Xeljanz oral solution

2. Prescriber is a Rheumatologist

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

4. 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

5. For **non-preferred agents** for polyarticular juvenile idiopathic arthritis:
    Actemra, Orencia (IV&SQ), Xeljanz tab, Xeljanz oral solution:
    a. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **BOTH** of the following preferred agents:
        i. Humira
        ii. Simponi Aria

    Enbrel:
    a. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **BOTH** of the following preferred agents:
        i. Humira
        ii. Simponi Aria
    b. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **ALL** of the following:
        i. Actemra
        ii. Orencia (IV or SQ)
        iii. Xeljanz and Xeljanz oral solution

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. **With first request for continuation:** Response is defined as AT LEAST a 30% improvement in JIA Core Set (see Definition section)
    b. **With subsequent request for continuation**: Documented evidence of disease stability and/or improvement with no evidence of disease progression

Renewal Duration: 12 months

Section F. 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, Rinvoq, Simponi, Simponi Aria, Skyrizi, Stelara, Taltz, Tremfya, Xeljanz tab, Xeljanz XR tab

2. Prescriber is a Rheumatologist or Dermatologist

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

4. 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, contraindication per FDA label, 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 per FDA label to methotrexate or NSAIDs

5. For Rinvoq, Xeljanz, Xeljanz XR **ONLY**:
    a. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to one or more TNF inhibitors (e.g., Cimzia, Humira, Simponi).

6. For **non-preferred agents** for psoriatic arthritis:
    Taltz:
    a. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **ONE** of the following preferred agents:
        i. Cimzia
        ii. Humira
        iii. Rinvoq
        iv. Simponi or Simponi Aria
        v. Skyrizi
        vi. Stelara
        vii. Tremfya
        viii. Xeljanz or Xeljanz XR

Orencia (IV&SQ)

a. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **TWO** of the following preferred agents:
    i. Cimzia
    ii. Humira
    iii. Rinvoq
    iv. Simponi or Simponi Aria
    v. Skyrizi
    vi. Stelara
    vii. Tremfya
    viii. Xeljanz or Xeljanz XR

Cosentyx, Enbrel:

a. **ALL** of the following:
    i. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **TWO** of the following preferred agents:
        1. Cimzia
        2. Humira
        3. Rinvoq
        4. Simponi or Simponi Aria
        5. Skyrizi
        6. Stelara
        7. Tremfya
        8. Xeljanz or Xeljanz XR
    ii. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **BOTH** of the following:
        1. Taltz
        2. Orencia (IV or 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. **With first request for continuation**: Response is defined as AT LEAST a 20% improvement in any of the following: ACR, CDAI, DAS28, PAS, PASII, RAPID-3, SDAI (see Definition section)
    b. **With subsequent request for continuation**: Documented evidence of disease stability and/or improvement with no evidence of disease progression

Renewal Duration: 12 months

BIOLOGIC AND IMMUNOLOGICAL AGENTS

Section G. 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 tab, Xeljanz XR tab

2. Prescriber is a Rheumatologist

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

4. 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

5. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **methotrexate**

6. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **ONE** of the following: [Note this criterion is waived if the individual already has tried an FDA-approved Rheumatoid Arthritis biologic]
    a. Leflunomide
    b. Sulfasalazine

7. For Rinvoq, Xeljanz, Xeljanz XR **ONLY**:
    a. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to one or more TNF inhibitors (e.g., Cimzia, Humira, Simponi).

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

Enbrel, Kevzara, Kineret, Olumiant:

a. **ALL** of the following:
   i. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **TWO** of the following preferred agents:
      1. Cimzia
      2. Humira
      3. Rinvoq
      4. Simponi or Simponi Aria
      5. Xeljanz tab or Xeljanz XR tab
   ii. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **BOTH** of the following:
      1. Actemra
      2. Orencia (IV or 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. **With first request for continuation**: Response is defined as AT LEAST a 20% improvement in any of the following: ACR, CDAI, DAS28, PAS, PASII, RAPID-3, SDAI (see Definition section)
   b. **With subsequent request for continuation**: Documented evidence of disease stability and/or improvement with no evidence of disease progression

Renewal Duration: 12 months

Section H. 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, Stelara, Xeljanz tab, Xeljanz XR tab

2. Prescriber is a Gastroenterologist

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

4. Diagnosis of moderate to severe active ulcerative colitis, as indicated by **ONE** of the following:
   a. American College of Gastroenterology Ulcerative Colitis activity index rating of moderate to severe disease in adults

b. Pediatric ulcerative colitis activity index (PUCAI) greater than or equal to 35

c. **At least 5** of the following signs and symptoms:
   i. Anemia
   ii. Bloody diarrhea or visible blood in stool
   iii. Bowel movements 4-6 or more times per day
   iv. Colicky abdominal pain
   v. Elevated fecal calprotectin
   vi. Elevated serum C-reactive protein or erythrocyte sedimentation rate
   vii. Fatigue
   viii. Fever
   ix. Tenesmus
   x. Urgency
   xi. Weight loss or delayed growth in children

5. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **ONE or more** of the following: [Note this criterion is waived if the individual already has tried an FDA-approved Ulcerative Colitis biologic]
   a. 6-mercaptopurine
   b. Azathioprine
   c. Oral corticosteroids
   d. Salicylates (such as mesalamine, sulfasalazine, balsalazide, olsalazine)

6. For **non-preferred agents** for ulcerative colitis (UC):
   Xeljanz tab, Xeljanz XR tab
   a. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to **TWO** of the following preferred agents:
      i. Humira
      ii. Simponi
      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. **With first request for continuation ONE of the following:**
      i. Response is defined as AT LEAST a 20% improvement in signs and symptoms of ulcerative colitis
      ii. American College of Gastroenterology Ulcerative Colitis activity index rating of mild disease or disease in remission in adults

iii. Pediatric ulcerative colitis activity index (PUCAI) of ≤ 34 in children indicating mild disease or disease remission

b. **With subsequent request for continuation**: Documented evidence of disease stability and/or improvement with no evidence of disease progression

Renewal Duration: 12 months

Section I. Behcet's Disease:

- **Criteria for initial therapy:** Otezla (apremilast) 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 (apremilast)

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. 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

5. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label 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

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

b. **With subsequent request for continuation**: Documented evidence of disease stability and/or improvement with no evidence of disease progression

Renewal duration: 12 months

Section J. Cytokine Release Syndrome:

- **Criteria for initial therapy:** Actemra 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 K. Moderate Giant Cell Arteritis:

- **Criteria for initial therapy:** Actemra 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. Diagnosis is confirmed by temporal artery biopsy
  5. Individual has failure (used for ≥ 3 consecutive months), contraindication per FDA label, or intolerance to glucocorticoids

  Approval Duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Actemra 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. **With first request for continuation:** Response is defined as AT LEAST 20% improvement in signs and symptoms of giant cell arteritis
    b. **With subsequent request for continuation**: Documented evidence of disease stability and/or improvement with no evidence of disease progression

Renewal duration: 12 months

Section L. Moderate to severe Hidradenitis Suppurativa:

- **Criteria for initial therapy:** Humira 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. 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

5. Individual has failure, contraindication per FDA label, 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):** Humira 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. **With first request for continuation:** Response is defined as AT LEAST a 20% improvement in the signs and symptoms of hidradenitis suppurativa
    b. **With subsequent request for continuation**: Documented evidence of disease stability and/or improvement with no evidence of disease progression

Renewal Duration: 12 months

Section M. Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD):

- **Criteria for initial therapy:** Actemra is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met for systemic sclerosis-associated interstitial lung disease:

  1. Request is for Actemra
  2. Prescriber is a Rheumatologist or Pulmonologist
  3. Meets other initial criteria per indication or use as described in Section A above
  4. Diagnosis is confirmed by meeting **ALL** of the following:
     a. Systemic sclerosis-interstitial lung disease as defined by American College of Rheumatology/European League Against Rheumatism
     b. Disease onset (first non-Raynaud symptom) is less than or equal to 5 years
     c. Modified Rodnan Skin Score (mRSS) of 10 or more but less than or equal to 35
     d. Elevated inflammatory markers (e.g., CRP, ERS) or platelets
     e. Active disease based on **one** of the following:
        i. Disease duration is less than or equal to 18-months
        ii. Increase in mRSS of greater than or equal to 3-units over 6-months
        iii. Involvement of one new body area and increase in mRSS of greater than or equal to 2-units over 6-months
        iv. Involvement of two new body areas over previous 6-months
        v. Presence of at least one tendon friction rub
  5. Individual has failure (used for ≥ 3 consecutive months), contraindication or intolerance to mycophenolate
  6. Will not be used in combination with Ofev (nintedanib)

  Approval Duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Actemra 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 **TWO** of the following:
        i. Improvement in mRSS over baseline of at least 4
        ii. Improvement or stabilization in FVC over baseline
        iii. Improvement or stabilization in percent predicted forced vital capacity (ppFVC) over baseline
        iv. Improvement or stabilization in DLCO
        v. Improved or no decline in symptoms for fatigue, cough or dyspnea

3. Individual has been adherent with the medication

4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
    a. Significant adverse effect such as:
        i. Liver toxicity

5. There are no significant interacting drugs

6. Will not be used in combination with Ofev (nintedanib)

Renewal duration: 12 months

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

- **Criteria for initial therapy:** Humira 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 has failure, contraindication per FDA label, 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, tacrolimus, sirolimus, or chlorambucil)

    Approval Duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Humira 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. **With first request for continuation:** Response is defined as AT LEAST a 20% improvement in the signs and symptoms of uveitis or panuveitis

b. **With subsequent request for continuation**: Documented evidence of disease stability and/or improvement with no evidence of disease progression

Renewal Duration: 12 months

Section O. 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

Section P. Other:

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-cancer Medications**

2. **Off-Label Use of Cancer Medications**

Definitions:

Adult: Age 18 years and older.

Preferred and Non-Preferred Agents:

Disease State	Preferred Agents	Non-Preferred Agents
Rheumatoid Arthritis (RA)	Cimzia* Humira* Rinvoq* Simponi* Simponi Aria† Xeljanz tab* Xeljanz XR tab*	Actemra (IV)† DSE Actemra (SQ)* DSE Enbrel* QSE Kevzara* QSE Kineret* QSE Olumiant* QSE Orencia (IV)† DSE Orencia (SQ)* DSE

BIOLOGIC AND IMMUNOLOGICAL AGENTS

Psoriatic Arthritis (PsA)	Cimzia* Humira* Otezla* Rinvoq* Simponi* Simponi Aria† Skyrizi* Stelara (IV)† Stelara (SQ)* Xeljanz tab* Xeljanz XR tab*	Cosentyx* QSE Enbrel* QSE Orencia (IV)† DSE Orencia (SQ)* DSE Taltz* SSE
Psoriasis (PsO)	Cimzia* Humira* Otezla* Skyrizi* Stelara (IV)† Stelara (SQ)* Tremfya*	Cosentyx* QSE Enbrel* QSE Siliq* QSE Taltz* SSE
Ankylosing Spondylitis	Cimzia* Humira* Simponi* Simponi Aria†	Cosentyx* TSE Enbrel* TSE Taltz* SSE Xeljanz tab* DSE Xeljanz XR tab* DSE
Juvenile Idiopathic Arthritis	Humira* Simponi Aria†	Actemra (IV)† DSE Actemra (SQ)* DSE Enbrel* QSE Orencia (IV)† DSE Orencia (SQ)* DSE Xeljanz oral solution* DSE
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.

***Pharmacy Benefit:** Injectable and oral medications that can be self-administered are billed and processed through pharmacy benefit only.
† **Medical Benefit:** Injectable medications that must be administered by a healthcare professional.

BIOLOGIC AND IMMUNOLOGICAL AGENTS

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	
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 ©	

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.	

Crohn's Disease Activity Index:
Sum each factor after adjustment with a weighting factor

Clinical or laboratory variable	Weighting factor	Factor Sum
Number of liquid or soft stools each day for seven days	x 2	
Abdominal pain (graded 0 = none, 1 = mild, 2 = moderate, 3 = severe) each day for 7 days	x 5	
General well-being (assessed from 0 = well, 1 = slightly under par, 2 = poor, 3 = very poor, 4 = terrible) each day for 7 days	x 7	
Presence of complications†	x 20	
Taking Lomotil (diphenoxylate/atropine) or opiates for diarrhea (0 = No, 1 = Yes)	x 30	
Presence of an abdominal mass (0 = none, 2 = questionable, 5 = definite)	x 10	
Hematocrit of < 0.47 in men and < 0.42 in women	x 6	
Percentage deviation from standard weight [1 – (ideal/observed)] x 100	x 1	

† **Complications**: one point each is added for each: • the presence of joint pains (arthralgia) or frank arthritis • inflammation of the iris or uveitis • presence of erythema nodosum, pyoderma gangrenosum, or aphthous ulcers • anal fissures, fistulae or abscesses • other fistulae • fever during the previous week	
Total CDAI	
Remission of CD: CDAI < 150 Severe CD: CDAI > 450 CD response: decrease in CDAI of > 70	

Pediatric Crohn disease activity index (PCDAI):

HISTORY: Recall from previous week		
Abdominal Pain	None	0 points
	Mild – Brief, does not interfere with activities	5 points
	Moderate or severe – Daily, longer lasting, affects activities, nocturnal	10 points
Stools (per day)	0-1 liquid stools, no blood	0 points
	Up to 2 semi-formed stools with small blood, or 2-5 liquid stools without blood	5 points
	Gross bleeding, or ≥6 liquid stools, or nocturnal diarrhea	10 points
Patient functioning, general well-being	No limitations of activities, well	0 points
	Occasional difficulty in maintaining age-appropriate activities, below par	5 points
	Frequent limitation of activity, very poor	10 points
Laboratory		
Hematocrit (%) <10 years	>33	0 points
	28 t32	2.5 points
	<28	5 points
Hematocrit (%) 11-19 years (females)	≥34	0 points
	29 to 33	2.5 points
	<29	5 points
Hematocrit (%) 11-14 years (males)	≥ 35	0 points
	30 to 34	2.5 points
	<30	5 points
Hematocrit (%) 15 to 19 years (male)	≥37	0 points
	32 to 36	2.5 points
	<32	5 points
ESR (mm/hour)	<20	0 points
	20 to 50	2.5 points
	>50	5 points
Albumin (g/dl)	≥3.5	0 points

	3.1 to 3.4	5 points
	≤3	10 points
Examination		
Weight	Weight gain, weight stable, or voluntary weight loss	0 points
	Involuntary weight stable, or weight loss 1 to 9%	5 points
	Weight loss ≥10%	10 points
Height (at diagnosis)	<1 channel decrease*	0 points
	1 to 2 channel decrease	5 points
	≥2 channel decrease	10 points
Height (at follow-up)	High velocity ≥-1 SD	0 points
	High velocity between -1 and -2 SD	5 points
	High velocity ≤-2 SD	10 points
Abdomen	No tenderness, no mass	0 points
	Tenderness, or mass without tenderness	5 points
	Tenderness, involuntary guarding, definite mass	10 points
Perirectal disease	None, asymptomatic tags	0 points
	1 to 2 indolent fistula(e), scant drainage, no tenderness	5 points
	Active fistula, drainage, tenderness, or abscess	10 points
Extraintestinal manifestations (Fever ≥38.5°C for 3 days over past week, definite arthritis, uveitis, erythema nodosum, pyoderma gangrenosum)	None	0 points
	1	5 points
	≥2	10 points

The PCDAI is interpreted as follows: a score of 0 to 10 indicates inactive disease, 11 to 30 indicates mild disease activity, and >30 indicates moderate to severe disease activity. A decrease in PCDAI of ≥12.5 points reflects a clinical response (improvement from moderate/severe to mild/inactive disease)
ESR: erythrocyte sedimentation rate; SD: standard deviation.
* A "channel decrease" refers to serial height measurements that deviate across the width of a major curve on a standard height-for-age chart. For example, decreasing from the 40th to 20th percentile is a 1-channel decrease.

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.

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

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].
© 2018 UpToDate, Inc. 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.*

American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) Classification Criteria for Systemic Sclerosis (SSc):

ACR-EULAR Criteria for the classification of Systemic Sclerosis		
These criteria are ***not*** applicable to: a) Patients having a SSc-like disorder better explaining their manifestations, such as: nephrogenic sclerosing fibrosis, generalized morphea, eosinophilic fasciitis, scleredema diabeticorum, scleromyxedema, erythromyalgia, porphyria, lichen sclerosis, graft versus host disease, and diabetic cheiropathy. b) Patients with `*Skin thickening sparing the fingers*' ***Patients having a total score of 9 or more are classified as having definite systemic sclerosis***		
Items	Sub-items	Weight score
Skin thickening of the fingers of both hands extending proximal to the metacarpophalangeal joints is a sufficient criterion to classify as having SSc		9
Skin thickening of the fingers	Puffy fingers	2

(only count the highest score)	Sclerodactyly of the fingers (distal to MCP but proximal to the PIPs)	4
Finger-tip lesions *(only count the highest score)*	Digital Tip Ulcers Finger Tip Pitting Scars	2 3
Telangiectasia		2
Abnormal nail-fold capillaries		2
Pulmonary arterial hypertension and/or Interstitial lung Disease (Maximum score is 2)	PAH ILD	2
Raynaud's phenomenon		3
Systemic sclerosis-related autoantibodies (any of anti-centromere, anti-topoisomerase I [anti-Sd 70], anti-RNA polymerase III) (Maximum score is 3)	Anti-centromere Anti-topoisomerase I Anti-RNA polymerase III	3
Total score		

PAH (pulmonary arterial hypertension) is defined as proven PAH by right heart catheterization

ILD (interstitial lung disease) is defined as pulmonary fibrosis on HRCT or chest radiograph, most pronounced in the basilar portions of the lungs, or presence of `velcro' crackles on auscultation not due to another cause such as congestive heart failure

Definitions of the SSc classification criteria items

Item	Definition
Skin thickening	Skin thickening or hardening not due to scarring after injury, trauma, etc.
Puffy fingers	Swollen digits - a diffuse, usually non-pitting increase in soft tissue mass of the digits extending beyond the normal confines of the joint capsule. Normal digits are narrowed distally with the tissues following the contours of the digital bone and joint structures. Swelling of the digits obliterates these contours. Not due to other reasons such as inflammatory dactylitis
Finger-tip ulcers or pitting scars	Ulcers or scars distal to or at the PIP joint not thought to be due to trauma. Digital pitting scars are depressed areas at digital tips as a result of ischemia, rather than trauma or exogenous causes.
Telangiectasia	Telangiectasia(e) in a scleroderma like pattern are round and well demarcated and found on hands, lips, inside of the mouth, and/or large matt-like telangiectasia(e). Telangiectasiae are visible macular dilated superficial blood vessels; which collapse upon pressure and fill slowly when pressure is released; distinguishable from rapidly filling spider angiomas with central arteriole and from dilated superficial vessels.
Abnormal nail-fold capillary pattern consistent with SSc	Enlarged capillaries and/or capillary loss with or without peri-capillary hemorrhages at the nail-fold and may be seen on the cuticle.
Pulmonary arterial hypertension	Pulmonary arterial hypertension diagnosed by right heart catheterization according to standard definitions.
Interstitial lung disease	Pulmonary fibrosis on HRCT or chest radiograph, most pronounced in the basilar portions of the lungs, or presence of `Velcro' crackles on auscultation not due to another cause such as congestive heart failure.

Raynaud's phenomenon	Self-report or reported by a physician with at least a two-phase color change in finger(s) and often toe(s) consisting of pallor, cyanosis and/or reactive hyperemia in response to cold exposure or emotion; usually one phase is pallor.
Systemic sclerosis-related autoantibodies	Anti-centromere antibody or centromere pattern on antinuclear antibody (ANA) testing; anti-topoisomerase I antibody (also known as anti-Scl70 antibody); or anti-RNA polymerase III antibody. Positive according to local laboratory standards.

Modified Rodnan Skin Score (mRSS):
Skin thickness assessment. The mRSS scores are rated as 0 = normal skin, 1 = mild thickness, 2 = moderate thickness, 3 = severe thickness with inability to pinch the skin into a fold across 17 different sites. The total score is the sum of the individual skin scores in the 17 body areas (e.g., face, anterior chest, abdomen, upper arm (left and right), forearm (left and right), hand (left and right), fingers (left and right), thigh (left and right), leg (left and right), and foot (left and right), giving a range of 0-51 units. It has been validated for participants with systemic sclerosis (SSc). A negative change from baseline indicates improvement.

Ulcerative Colitis Activity (Adults):

American College of Gastroenterology Ulcerative Colitis Activity Index				
	Remission	Mild	Moderate-severe	Fulminant
Stools (no./d)	Formed	< 4	> 6	> 10
Blood in stools	None	Intermittent	Frequent	Continuous
Urgency	None	Mild, occasional	Often	Continuous
Hemoglobin	Normal	Normal	< 75% of normal	Transfusion needed
ESR	< 30	< 30	> 30	> 30
CRP (mg/L)	Normal	Elevated	Elevated	Elevated
Fecal calprotectin (mg/g)	< 150-200	> 150-200	> 150-200	> 150-200
Endoscopy (Mayo sub-score)	0-1	1	2-3	3
UCEIS	0-1	2-4	5-8	7-8
The above factors are general guides for disease activity. With the exception of remission, a patient does not need to have all the factors to be considered in a specific category. CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; UCEIS, Ulcerative Colitis Endoscopic Index of Severity.				

Endoscopic Assessment of Disease Activity		
Endoscopic Features	UCEIS Score	Mayo Score
Normal	0	0
Erythema, decreased vascular pattern, mild friability	1-3	1
Marked erythema, absent vascular pattern, friability, erosions	4-6	2
Spontaneous bleeding, ulceration	7-8	3

Pediatric ulcerative colitis activity index (PUCAI)

Abdominal pain	No pain	0 points
	Pain can be ignored	5 points
	Pain cannot be ignored	10 points
Rectal Bleeding	None	0 points
	Small amount only, in <50% of stools	10 points
	Small amount with most stools	20 points

	Large amount (>50% of the stool content)	30 points
Stool consistency of most stools	Formed	0 points
	Partially formed	5 points
	Completely unformed	10 points
Number of stools er 24 hours	0 to 2	0 points
	3 to 5	5 points
	6 to 8	10 points
	>8	15 points
Nocturnal stools (any episode causing wakening)	No	0 points
	Yes	10 points
Activity level	No limitation of activity	0 points
	Occasional limitation of activity	5 points
	Severe restricted activity	10 points
Sum (0-85) PUCAI scores are interpreted as follows: 0 to 9 – Remission 10 to 34 – Mild disease 35 to 64 – Moderate disease 65 to 85 – Severe disease		

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

Resources:

2.04.84 BCBS Association Medical Policy Reference Manual. Measurement of Serum Antibodies to Selected Biologic Agents. Re-issue date 11/12/2020, issue date 08/09/2012. Accessed October 28, 2021.

Actemra (tocilizumab) injection product information, revised by Genentech, Inc. 03-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2021.

Cimzia (certolizumab) injection product information, revised by UCB, Inc. 09-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2021.

Cosentyx (secukinumab) injection product information, revised by Novartis Pharmaceuticals Corporation 05-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2021.

Enbrel (etanercept) injection product information, revised by Immunex Corporation 04-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2021.

BIOLOGIC AND IMMUNOLOGICAL AGENTS

Humira (adalimumab) injection product information, revised by AbbVie Inc. 02-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2021.

Kevzara (sarilumab) injection product information, revised by Sanofi-Aventis U.S. LLC. 04-2018. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2021.

Kineret (anakinra) injection product information, revised by Swedish Orphan Biovitrum AB (publ) 12-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2021.

Olumiant (baricitinib) product information, revised by Eli Lilly and Company12-2021.. Available at DailyMed http://dailymed.nlm.nih.gov. AccessedFebruary 1, 2022..

Orencia (abatacept) injection product information, revised by E.R. Squibb & Sons, LLC. 06-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2021.

Otezla (apremilast) product information, revised by Celgene Corporation 07-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2021.

Rinvoq (upadactinib) product information, revised by AbbVie Inc. 01-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 1, 2022.

Siliq (brodalumab) injection product information, revised by Bausch Health US LLC. 04-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2021.

Simponi (golimumab) injection product information, revised by Janssen Biotech, Inc. 09-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2021.

Simponi Aria (golimumab) injection product information, revised by Janssen Biotech, Inc. 02-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2021.

Skyrizi (Risankizumab) Injection product information, revised by AbbVie Inc.01-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 1, 2022..

Stelara (ustekinumab) injection product information, revised by Janssen Biotech, Inc. 12-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2021.

Taltz (ixekizumab) injection product information, revised by Eli Lilly and Company 03-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2021.

Tremfya (guselkumab) injection product information, revised by Janssen Biotech, Inc. 07-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed October 17, 2021.

Xeljanz (tofacitinib) tab, Xeljanz (tofacitinib) oral solution, and Xeljanz XR (tofacitinib) tab product information, revised by Pfizer Laboratories Div Pfizer Inc. 12-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 1, 2022.

BIOLOGIC AND IMMUNOLOGICAL AGENTS

Yu DT, van Tubergen A. Diagnosis and differential diagnosis of axial spondyloarthritis (ankylosing spondylitis and nonradiographic axial spondylarthritis) in adults. In: UpToDate, Sieper J, Romain RL (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 18, 2021.

Yu DT, van Tubergen A. Treatment of axial spondylarthritis (ankylosing spondylitis and nonradiographic axial spondyloarthritis in adults. In: UpToDate, Sieper J, Romain RL (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 16, 2021.

Smith EL, Yazici Y. Clinical manifestations and diagnosis of Bachet syndrome. In: UpToDate, Merkel PA, Curtis MR (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed October 18, 2021.

Smith EL, Yazici Y. Treatment of Bachet syndrome. In: UpToDate, Merkel PA, Curtis MR (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed October 18, 2021.

Setty M, Russell GH, Bousvaros Athos. Clinical manifestations and complications of inflammatory bowel disease in children and adolescents. In: UpToDate, Motil KJ, Heyman MB, Hoppin AG (Eds), UpToDate, Waltham, MA. : UpToDate Inc. Available at http://uptodate.com. Accessed September 17, 2021.

Peppercorn MA, Kane SV. Clinical manifestations, diagnosis, and prognosis of Crohn disease in adults. In: UpToDate, Lamont JT, Robson KM (Eds), UpToDate, Waltham, MA. : UpToDate Inc. Available at http://uptodate.com. Accessed September 17, 2021.

Hashash JA, Reguerio M. Overview of medical management of high-risk, adult patients with moderate to severe Crohn disease. In: UpToDate, Kane SV, Robson KM (Eds), UpToDate, Waltham, MA. : UpToDate Inc. Available at http://uptodate.com. Accessed September 17, 2021.

Zitomersky N, Bousvaros A. Overview of the management of Crohn disease in children and adolescents. In: UpToDate, Motil, KJ, Heyman MB, Hoppin AG (Eds), UpToDate, Waltham, MA. : UpToDate Inc. Available at http://uptodate.com. Accessed September 21, 2021.

Armstrong AW. Treatment Selection for moderate to severe plaque psoriasis in special populations. In UpToDate, Duffin KC, Ofori AO (Eds), UpToDate, Waltham, MA. : UpToDate Inc. Available at http://uptodate.com. Accessed September 17, 2021.

Feldman SR. Treatment of psoriasis in adults. In: UpToDate, Dellavalle RP, Duffin KC, Ofori, AO (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 17, 2021.

Gladman DD, Ritchlin C. Treatment of psoriatic arthritis. In UpToDate, Sieper J, Romain PL (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 17, 2021.

Moreland LW, Cannella A. General principles and overview of management of rheumatoid arthritis in adults. In: UpToDate, Romain PL (Ed), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 16, 2021.

BIOLOGIC AND IMMUNOLOGICAL AGENTS

Cohen S, Mikuls TR. Initial treatment of rheumatoid arthritis in adults. In: UpToDate, O'Dell JR, Romain PL (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 16, 2021.

Smolen JS, Aletaha D. Assessment of rheumatoid arthritis disease activity and physical function. In: UpToDate, St Clair EW, Romain PL (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 16, 2021.

Cohen S, Cannella A. Treatment of rheumatoid arthritis in adults resistant to initial conventional nonbiologic DMARD therapy. In: UpToDate, O'Dell JR, Romain PL (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 16, 2021.

Peppercorn MA, Kane SV. Clinical manifestations, diagnosis, and prognosis of ulcerative colitis in adults. In: UpToDate, Lamont JT, Robson KM (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 21, 2021.

Cohen RD, Stein AC. Management of moderate to severe ulcerative colitis in adults. In: UpToDate, Kane SV, Robson KM (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 21, 2021.

Bousvaros A, Setty M, Kaplan JL. Management of mild to moderate ulcerative colitis in children and adolescents. In: UpToDate, Heyman MB, Hoppin AG (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 21, 2021.

Bousvaros A, Setty M, Kaplan JL. Management of severe or refractory ulcerative colitis in children and adolescents. In: UpToDate, Heyman MB, Hoppin AG (Eds), UpToDate, Waltham, MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 21, 2021.

Porter DL, Maloney DG. Cytokine release syndrome (CRS). In: UpToDate, Negrin RS, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed October 18, 2021.

Docken WP. Diagnosis of giant cell arteritis. In: UpToDate, Trobe J, Matteson EL, Curtis MR (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed October 18, 2021.

Docken WP. Treatment of giant cell arteritis. In: UpToDate, Trobe J, Matteson EL, Curtis MR (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed October 18, 2021.

Ingram JR. Hidradenitis suppurativa: Pathogenesis, clinical features, and diagnosis. In: UpToDate, Dellavalle RP, Owen C, Ofori OA (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed October 18, 2021.

Ingram JR. Hidradenitis suppurativa: Management. In: UpToDate, Dellavalle RP, Owen C, Ofori OA (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed October 18, 2021.

Rosenbaum JT. Uveitis: Etiology, clinical manifestations, and diagnosis. In: UpToDate, Thorne JE, Romain PL (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed October 18, 2021.

BIOLOGIC AND IMMUNOLOGICAL AGENTS

Rosenbaum JT. Uveitis: Treatment. In: UpToDate, Thorne JE, Romain PL (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed October 18, 2021.

Weiss PF. Polyarticular juvenile idiopathic arthritis: Clinical manifestations, diagnosis, and complications. In: UpToDate, Klein-Gitelman M, TePas E (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed October 18, 2021.

Weiss PF. Polyarticular juvenile idiopathic arthritis: Treatment. In: UpToDate, Klein-Gitelman M, TePas E (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed October 18, 2021.

Varga J. Clinical manifestations and diagnosis of systemic sclerosis (scleroderma) in adults. In: UpToDate, Axford JS, Curtis MR (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed June 10, 2021.

Denton CP. Overview of the treatment and prognosis of systemic sclerosis (scleroderma) in adults. In: UpToDate, Axford JS, Curtis MR, Hollingsworth H (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed June 10, 2021.

Varga J. Overview of pulmonary complications of systemic sclerosis (scleroderma) in adults. In: UpToDate, King TE, Axford JS, Curtis R (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed June 10, 2021.

Varga J. Clinical manifestations, evaluations, and diagnosis of interstitial lung disease in systemic sclerosis (scleroderma). In: UpToDate, King TE, Axford JS, Curtis R (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed June 10, 2021.

Varga J, Montesi S. Tretamnt and prognosis of interstitial lung disease in systemic sclerosis (scleroderma). In: UpToDate, King TE, Axford JS, Curtis R, Hollingswoth H (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed June 10, 2021.