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Biologic Immunomodulators Prior Authorization with Quantity Limit Program Summary

FDA APPROVED INDICATIONS AND DOSAGE[1-16,43,44]

Agent(s)	Indication(s)	Dosage
Actemra® (tocilizumab) Intravenous infusion Subcutaneous injection	Treatment of adult patients with moderate to severely active rheumatoid arthritis (RA) who have hand an inadequate response to one or more disease-modifying anti-rheumatic drugs Treatment of giant cell arteritis (GCA) in adult patients Treatment of active polyarticular juvenile idiopathic arthritis (PJIA) in patients 2 years of age and older Treatment of active systemic juvenile idiopathic arthritis (SJIA) in patients 2 years of age and older Treatment of chimeric antigen receptor (CAR) T-cell included severe or life-threatening cytokine release syndrome (CRS) in adults and pediatric patients 2 years of age and older Slowing the rate of decline in pulmonary function in adult patients with systemic sclerosis associated interstitial lung disease (SSc-ILD) Limitation of use: SC administration with the prefilled ACTPen autoinjector and IV administration has not been studied in SSc-ILD	**RA IV:** 4 mg/kg IV over 60 min every 4 weeks, may increase to 8 mg/kg every 4 weeks **RA SC:** • weight <100 kg: 162 mg every 2 weeks, may increase to weekly • weight ≥100 kg: 162 mg once weekly **GCA IV:** 6 mg/kg IV over 60 min every 4 weeks in combination with tapering course of glucocorticoids Doses exceeding 600 mg per infusion are not recommended in GCA patients **GCA SC**: 162 mg once weekly, in combination with a tapering course of glucocorticoids, every 2-week dosing may be considered **PJIA IV**: IV over 60 min every 4 weeks • weight <30 kg: 10 mg/kg • weight ≥30 kg: 8 mg/kg **PJIA SC:** • weight <30 kg: 162 mg every 3 weeks • weight ≥30 kg: 162 mg every 2 weeks **SJIA IV:** IV over 60 min every 2 weeks • weight <30 kg: 12 mg/kg • weight ≥30 kg: 8 mg/kg **SJIA SC**: • weight <30 kg: 162 mg every 2 weeks • weight ≥30 kg: 162 mg once weekly **CRS IV:** IV over 60 min for up to 4 doses with interval between consecutive doses of at least 8 hours, not to exceed 800mg per infusion • weight <30 kg: 12 mg/kg • weight ≥30 kg: 8 mg/kg

		SSc-ILD: 162 mg SC once weekly
Cimzia® (certolizumab pegol) Subcutaneous injection	Reducing signs and symptoms of Crohn's disease (CD) and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy Treatment of adults with moderately to severely active rheumatoid arthritis (RA) Treatment of adult patients with active psoriatic arthritis (PSA) Treatment of adults with active ankylosing spondylitis (AS) Treatment of adults with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation Treatment of adults with moderate-to-severe plaque psoriasis (PS) who are candidates for systemic therapy or phototherapy	**CD:** 400 mg SC at day 0, week 2, and week 4, then 400 mg every 4 weeks **RA:** 400 mg SC at day 0, week 2 and 4, then 200 mg every 2 weeks or 400 mg every 4 weeks **PSA:** 400 mg SC at day 0, week 2 and 4, then 200 mg every 2 weeks or 400 mg every 4 weeks **AS**: 400 mg SC at day 0, week 2, and week 4, then 200 mg every 2 weeks or 400 mg every 4 weeks **nr-axSpA**: 400 mg SC at day 0, week 2, and week 4, then 200 mg every 2 weeks or 400 mg every 4 weeks **PS**: 400 mg every 2 weeks; for some patients (body weight ≤90 kg) 400 mg SC at day 0, week 2, and week 4, then 200 mg every 2 weeks can be considered
Cosentyx® (secukinumab) Subcutaneous injection	Treatment of moderate to severe plaque psoriasis (PS) in patients 6 years and older who are candidates for systemic therapy or phototherapy Treatment of active psoriatic arthritis (PSA) in patients 2 years of age and older Treatment of adult patients with active ankylosing spondylitis (AS) Treatment of adult patients with active non-radiographic	**Adult PS, PSA with coexisting PS:** 300 mg SC at weeks 0, 1, 2, 3, and 4, then 300 mg every 4 weeks or 150 mg every 4 weeks. **Pediatric PS**: weight-based dosing SC at weeks 0, 1, 2, 3, and 4, then every 4 weeks thereafter • <50 kg: 75 mg • ≥50 kg: 150 mg **Adult PSA:** • **With loading dose:** 150 mg SC at weeks 0, 1, 2, 3, and 4, then every 4 weeks thereafter • **Without loading dose:** 150 mg SC every 4 weeks

	axial spondyloarthritis (nr-ax-SpA) with objective signs of inflammation Treatment of active enthesitis-related arthritis (ERA) in patients 4 years of age and older	• May consider 300 mg for patients that continue to have active PSA **Pediatric PSA:** weight-based dosing SC at weeks 0, 1, 2, 3, and 4, then every 4 weeks thereafter • Weight ≥15 kg to <50 kg: 75 mg • Weight ≥50 kg: 150 mg **AS:** • **With loading dose:** 150 mg SC at weeks 0, 1, 2, 3, and 4, then every 4 weeks thereafter • **Without loading dose:** 150 mg SC every 4 weeks • May consider 300 mg for patients that continue to have active AS **nr-ax-SpA:** • **With loading dose:** 150 mg SC at weeks 0, 1, 2, 3, and 4, then every 4 weeks thereafter • **Without loading dose:** 150 mg SC every 4 weeks **ERA:** weight-based dosing SC at weeks 0, 1, 2, 3, and 4, then every 4 weeks thereafter • Weight ≥15 kg to <50 kg: 75 mg • Weight ≥50 kg: 150 mg
Enbrel® (etanercept) Subcutaneous injection	Reduce the signs and symptoms, including major clinical response, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis (RA) Reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis (PJIA) in patients ages 2 and older Reducing signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical	**RA:** 50 mg SC weekly **PJIA:** • weight <63 kg: 0.8 mg/kg SC weekly • weight ≥63 kg: 50 mg SC weekly **PSA:** 50 mg SC weekly **AS:** 50 mg SC weekly **Adult PS:** 50 mg SC twice weekly for 3 months, then 50 mg SC weekly **Pediatric PS:** • weight <63 kg: 0.8 mg/kg SC weekly • weight ≥63 kg: 50 mg SC weekly

	function in patients with psoriatic arthritis (PSA) Reducing signs and symptoms in patients with active ankylosing spondylitis (AS) Treatment of patients 4 years or older with chronic moderate to severe plaque psoriasis (PS) who are candidates for systemic therapy or phototherapy	
Humira® (adalimumab) Subcutaneous injection	Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis (RA) Reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis (PJIA) in patients 2 years of age and older Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active psoriatic arthritis (PSA) Reducing signs and symptoms in adult patients with active ankylosing spondylitis (AS) Treatment of moderately to severely active Crohn's disease (CD) in adults and pediatric patients 6 years of age and older Treatment of moderately to severely active ulcerative colitis (UC) in adults and	**RA:** 40 mg SC every 2 weeks; those with RA not on methotrexate may increase to 40 mg weekly or 80 mg every 2 weeks **PJIA:** • weight 10 kg to <15 kg: 10 mg SC every 2 weeks • weight 15 kg to <30 kg: 20 mg SC every 2 weeks • weight ≥30 kg: 40 mg SC every 2 weeks **PSA:** 40 mg SC every 2 weeks; those with RA not on methotrexate may increase to 40 mg weekly or 80 mg every 2 weeks **AS:** 40 mg SC every 2 weeks; those with RA not on methotrexate may increase to 40 mg weekly or 80 mg every 2 weeks **Adult CD, UC:** 160 mg SC on day 1, 80 mg on day 15, then 40 mg every 2 weeks starting on day 29 **Pediatric CD:** • weight 17 kg to <40 kg: 80 mg SC on day 1, 40 mg on day 15, then 20 mg every 2 weeks starting on day 29 • weight ≥40 kg: 160 mg SC on day 1, 80 mg on day 15, then 40 mg every 2 weeks starting on day 29 **Pediatric UC:** • weight 20 kg to <40 kg: 80 mg SC on day 1, 40 mg on days 8 and 15, then 20 mg every week or 40 mg every other week starting on day 29

	pediatric patients 5 years of age and older Limitation of use: The effectiveness of Humira has not been established in patients with UC who have lost response to or were intolerant to TNF blockers Treatment of adult patients with moderate to severe chronic plaque psoriasis (PS) who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate Treatment of moderate to severe hidradenitis suppurativa (HS) in patients 12 years of age and older Treatment of non-infectious intermediate, posterior, and panuveitis in adults and pediatric patients 2 years of age and older	• weight ≥40 kg: 160 mg SC on day 1, 80 mg on days 8 and 15, then 40 mg every week or 80 mg every other week starting on day 29 **Adult HS:** 160 mg SC on day 1, 80 mg on day 15, then 40 mg every week or 80 mg every 2 weeks starting on day 29 **Pediatric HS:** • weight 30 kg to <60 kg: 80 mg SC on day 1, then 40 mg every 2 weeks starting on day 8 • weight ≥60 kg: 160 mg SC on day 1, 80 mg on day 15, then 40 mg every week or 80 mg every 2 weeks starting on day 29 **PS, Adult uveitis:** 80 mg SC day 0, then 40 mg every 2 weeks starting one week after the initial dose **Adolescent uveitis:** • weight 10 kg to <15 kg: 10 mg SC every 2 weeks • weight 15 kg to <30 kg: 20 mg SC every 2 weeks • weight ≥30 kg: 40 mg SC every 2 weeks
Kevzara® (sarilumab) Subcutaneous injection	Treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs)	**RA:** 200 mg SC once every 2 weeks
Kineret® (anakinra) Subcutaneous injection	Reduction in signs and symptoms and slowing the progression of structural damage in moderately to severely active rheumatoid arthritis (RA), in patients 18 years of age or older who have failed 1 or more disease modifying antirheumatic drugs (DMARDs) Treatment of Neonatal-Onset Multisystem	**RA:** 100 mg SC daily **NOMID:** 1-2 mg/kg SC daily; maximum 8 mg/kg daily **DIRA:** initial dose of 1-2 mg/kg SC daily, titrated up in 0.5-1 mg/kg increments to a max of 8 mg/kg daily

	Inflammatory Disease (NOMID)[c] Treatment of Deficiency of Interleukin-1 Receptor Antagonist (DIRA)[c]	
Olumiant® (baricitinib) Oral tablet	Treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more tumor necrosis factor (TNF) blockers Limitation of Use: Not recommended for use in combination with other JAK inhibitors, biologic disease modifying antirheumatic drugs (DMARDs), or with potent immunosuppressants such as azathioprine and cyclosporine	**RA:** 2 mg orally per day
Orencia® (abatacept) Intravenous infusion Subcutaneous injection	Treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) Treatment of patients 2 years of age and older with moderately to severely active polyarticular juvenile idiopathic arthritis (PJIA) Treatment of adult patients with active psoriatic arthritis (PSA) Prophylaxis of acute graft versus host disease (aGVHD), in combination with calcineurin inhibitor and methotrexate, in adults and pediatric patients 2 years of age and older undergoing hematopoietic stem cell transplantation (HSCT) from a matched or 1 allele-mismatched unrelated-donor Limitation of Use: concomitant use with other	**RA IV:** IV over 30 min given at 0, 2, and 4 weeks, then every 4 weeks thereafter • weight <60 kg: 500 mg • weight 60 kg to 100 kg: 750 mg • weight >100 kg: 1000 mg **RA SC:** 125 mg once weekly, with or without IV loading dose **PJIA IV:** IV over 30 min given at 0, 2, and 4 weeks, then every 4 weeks thereafter • weight <75 kg: 10 mg/kg • weight ≥75 kg: same as adult RA/PSA IV dosing noted above, not to exceed 1000 mg **PJIA SC**: without the need for IV loading dose • weight 10 kg to <25 kg: 50 mg weekly • weight 25 kg to <50 kg: 87.5 mg weekly weight ≥50 kg: 125 mg weekly **PSA SC**: 125 mg once weekly without the need for an IV loading dose

	potent immunosuppressants (e.g., biologic disease modifying antirheumatic drugs [bDMARDS], Janus kinase [JAK]inhibitors) is not recommended	**PSA IV:** IV over 30 min given at 0, 2, and 4 weeks, then every 4 weeks thereafter • weight <60 kg: 500 mg • weight 60 kg to 100 kg: 750 mg weight >100 kg: 1000 mg **aGVHD IV**: IV infusion over 60 minutes • 6 years and older: 10 mg/kg (max of 1000 mg) on the day before transplantation (day 1), followed by administration on days 5, 14, and 28 after transplantation • 2 to less than 6 years: 15 mg/kg (max of 1000 mg) on the day before transplantation (day 1), followed by 12 mg/kg administration on days 5, 14, and 28 after transplantation
Rinvoq™ (upadacitinib extended release) Oral tablet	Treatment of adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more TNF blockers Treatment of adults with active psoriatic arthritis (PSA) who have had an inadequate response or intolerance to one or more TNF blockers Treatment of adult and pediatric patients 12 years of age and older with refractory, moderate to severe atopic dermatitis (AD) whose disease is not adequately controlled with other systemic drug products, including biologics, or when use of those therapies are inadvisable Treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response or intolerance to one or more TNF blockers	**PSA, RA:** 15 mg orally once daily **AD**: 12 years of age weighing at least 40 kg to less than 65 years of age: • 15 mg once daily, may consider increasing dose to 30 mg daily if adequate response is not achieved • Discontinue if adequate response is not achieved with 30 mg dose Adults 65 years of age and older: 15 mg once daily **UC**: • Induction: 45 mg once daily for 8 weeks • Maintenance: 15 mg once daily. A dose of 30 mg once daily may be considered for patients with refractory, severe or extensive disease. Discontinue if an adequate therapeutic response is not achieved with the 30 mg dose. Use lowest effective dose to maintain response.

	Limitation of Use: use in combination with other JAK inhibitors, biologic DMARDs, or with potent immunosuppressants such as azathioprine and cyclosporine, is not recommended	
Siliq™ (brodalumab) Subcutaneous injection	Treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies	**PS:** 210 mg SC given at 0, 1, and 2 weeks, followed by 210 mg every 2 weeks
Simponi® (golimumab) Subcutaneous injection	Treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) in combination with methotrexate Treatment of adult patients with active psoriatic arthritis (PSA) Treatment of adult patients with active ankylosing spondylitis (AS) Adult patients with moderately to severely active ulcerative colitis who have demonstrated corticosteroid dependence or who have had an inadequate response to or failed to tolerate oral aminosalicylates, oral corticosteroids, azathioprine, or 6-mercaptopurine	**AS, PSA, RA**: 50 mg SC once monthly **UC**: 200 mg SC at week 0, 100 mg at week 2, then 100 mg every 4 weeks
Skyrizi™ (risankizumab-rzaa) Subcutaneous injection	Treatment of moderate-to-severe plaque psoriasis (PS) in adults who are candidates for systemic therapy or phototherapy Treatment of active psoriatic arthritis (PSA) in adults	**PS, PSA:** 150 mg SC at weeks 0 and 4, then every 12 weeks thereafter
Stelara® (ustekinumab)	Treatment of patients 6 years and older with moderate to severe plaque	**Pediatric PS SC:** given at 0 and 4 weeks, then every 12 weeks • weight <60 kg: 0.75 mg/kg

Intravenous infusion Subcutaneous injection	psoriasis (PS) who are candidates for phototherapy for systemic therapy Treatment of adult patients with active psoriatic arthritis (PSA) Treatment of adult patients with moderately to severely active Crohn's disease (CD) Treatment of adult patients with moderately to severely active ulcerative colitis (UC)	• weight 60 kg to 100 kg: 45 mg • weight >100 kg: 90 mg **Adult PS SC:** given at 0 and 4 weeks, then every 12 weeks • weight ≤100 kg: 45 mg • weight >100 kg: 90 mg **PSA SC:** 45 mg at 0 and 4 weeks, then every 12 weeks **Adult PS with PSA SC**: weight >100 kg: 90 mg at 0 and 4 weeks, then every 12 weeks **CD IV:** IV over 60 min single induction infusion • weight ≤55 kg: 260 mg • weight >55 kg to 85 kg: 390 mg • weight >85 kg: 520 mg **CD SC:** 90 mg SC 8 weeks after initial IV induction, then every 8 weeks thereafter **UC IV:** IV over 60 min single induction infusion • weight ≤55 kg: 260 mg • weight >55 kg to 85 kg: 390 mg • weight >85 kg: 520 mg **UC SC:** 90 mg SC 8 weeks after initial IV induction, then every 8 weeks thereafter
Taltz® (ixekizumab) Subcutaneous injection	Treatment of patients 6 years of age and older with moderate-to severe plaque psoriasis who are candidates for systemic therapy or phototherapy Treatment of adult patients with active psoriatic arthritis Treatment of adult patients with active ankylosing spondylitis (AS) Treatment of adult patents with active non-radiographic axial spondyloarthritis (re-axSpA) with objective signs of inflammation	**Adult PS, Adult PS with PSA**: 160 mg SC at week 0, 80 mg at weeks 2, 4, 6, 8, 10, and 12, then 80 mg every 4 weeks **Pediatric (6 to <18 years) PS**: starting dose given at week 0, then every 4 weeks (patients weighing 50 kg or less, doses must be prepared and administered by a health care professional; use prefilled syringe only) • Weight >50 kg: 160 mg, then 80 mg • Weight 25 to 50 kg: 80 mg, then 40 mg • Weight <25 kg: 40 mg, then 20 mg **PSA**: 160 mg SC at week 0, then 80 mg every 4 weeks **AS:** 160 mg SC at week 0, then 80 mg every 4 weeks

		nr-axSpA: 80 mg SC every 4 weeks
Tremfya® (guselkumab) Subcutaneous injection	Treatment of adults with moderate-to-severe plaque psoriasis (PS) who are candidates for systemic therapy or phototherapy Treatment of adult patients with active psoriatic arthritis (PSA)	**PS, PSA:** 100 mg SC at 0 and 4 weeks, then every 8 weeks thereafter
Xeljanz® (tofacitinib) Oral tablet	Treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more TNF blockers Treatment of adult patients with active psoriatic arthritis (PSA) who have had an inadequate response or intolerance to one or more TNF blockers Treatment of adult patients with active ankylosing spondylitis (AS) who have had an inadequate response or intolerance to one or more TNF blockers Treatment of adult patients with moderately to severely active ulcerative colitis (UC), who have had an inadequate response or intolerance to one or more TNF blockers Treatment of active polyarticular course juvenile idiopathic arthritis (pcJIA) in patients 2 years of age and older who have had an inadequate response or intolerance to one or more TNF blockers Limitation of use: use of Xeljanz in combination with biologics DMARDs or with potent immunosuppressants	**pcJIA:** 10 kg to <20 kg: 3.2 mg oral solution twice daily 20 kg to <40 kg: 4 mg oral solution twice daily ≥40 kg: 5 mg (tablet or oral solution) twice daily **AS, PSA, RA:** 5 mg orally twice daily **UC**: 10 mg orally twice daily for 8 weeks (may continue for a max of 16 weeks), then 5 mg twice daily. Discontinue after 16 weeks of 10mg twice daily, if adequate therapeutic benefit is not achieved

	such as azathioprine and cyclosporine is not recommended	
Xeljanz® (tofacitinib) Oral solution	Treatment of active polyarticular course juvenile idiopathic arthritis (pcJIA) in patients 2 years of age and older who have had an inadequate response or intolerance to one or more TNF blockers Limitation of use: use of Xeljanz in combination with biologics DMARDs or with potent immunosuppressants such as azathioprine and cyclosporine is not recommended	**pcJIA:** 10 kg to <20 kg: 3.2 mg oral solution twice daily 20 kg to <40 kg: 4 mg oral solution twice daily ≥40 kg: 5 mg (tablet or oral solution) twice daily
Xeljanz® XR (tofacitinib extended release) Oral tablet	Treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to one or more TNF blockers Treatment of adult patients with active psoriatic arthritis (PSA) who have had an inadequate response or intolerance to one or more TNF blockers Treatment of adult patients with active ankylosing spondylitis (AS) who have had an inadequate response or intolerance to one or more TNF blockers Treatment of adult patients with moderately to severely active ulcerative colitis (UC), who have had an inadequate response or intolerance to one or more TNF blockers Limitation of use: use of Xeljanz XR in combination with biologics DMARDs or with potent	**AS, PSA, RA:** 11 mg orally once daily **UC:** 22 mg once daily for at least 8 weeks. Evaluate response and transition to maintenance therapy, if needed may continue for a maximum of 16 weeks, then maintenance dose of 11 mg once daily

	immunosuppressants such as azathioprine and cyclosporine is not recommended	

c – approved for use in pediatric patients as young as 1 month of age

CLINICAL RATIONALE
RHEUMATOID DISORDERS

Ankylosing spondylitis (AS)[17,47]

Ankylosing spondylitis (AS) is a form of chronic inflammatory arthritis characterized by sacroiliitis, enthesitis, and a marked propensity for sacroiliac joint and spinal fusion. AS is distinguished by universal involvement with sacroiliac joint inflammation or fusion and more prevalent spinal ankylosis. Goals of treatment for AS are to reduce symptoms, maintain spinal flexibility and normal posture, reduce functional limitations, maintain work ability, and decrease disease complications. The mainstays of treatment have been nonsteroidal anti-inflammatory drugs (NSAIDs) and exercise, with the additional use of disease-modifying antirheumatic drugs (DMARDs) in patients with peripheral arthritis. The American College of Rheumatology (ACR), Spondylitis Association of America (SAA), and Spondyloarthritis Research and Treatment Network (SPARTAN) recommend the following pharmacological treatment for AS:

- Stable AS: First line therapy with on demand NSAIDs; there is also a conditional recommendation for continuation of TNF inhibitor as monotherapy
- Active AS:
  - First line therapy with continuous NSAIDs with physical therapy
  - TNF inhibitor recommended for patients with active AS despite an adequate trial with NSAIDs
    - Lack of response (or intolerance) to at least 2 different NSAIDs over 1 month or incomplete response to at least 2 different NSAIDs over 2 months would be an adequate NSAID trial to judge response
  - Recommendations for nonresponse to TNF therapy (all conditional):
    - Primary nonresponse: switch to secukinumab or ixekizumab over another TNF
    - Secondary nonresponse: switch to another TNF over a non-TNF biologic
    - Recommend against addition of sulfasalazine or MTX
    - Recommend against switching to a biosimilar of the failed TNF
  - TNF-inhibitors are conditionally recommended over secukinumab or ixekizumab
  - Secukinumab or ixekizumab are conditionally recommended over DMARDs in patients that have failed NSAIDs and have contraindications to TNF-inhibitors
  - DMARDs (i.e., methotrexate [MTX], sulfasalazine) are only conditionally recommended in patients that have failed NSAIDs and have contraindications to TNF-inhibitors
  - Methotrexate is not recommended as add on therapy to TNF inhibitors in stable and active AS
  - If patient has concomitant inflammatory bowel disease (IBD) or recurrent uveitis, TNF-inhibitors are recommended over other biologics
  - Glucocorticoids are not recommended

Nonradiographic Axial Spondyloarthritis (nr-axSpA)[17,47]

Nonradiographic axial spondyloarthritis (nr-axSpA) falls under the same spondyloarthritis family as ankylosing spondylitis (AS). Nr-axSpA includes patients with chronic back pain and features suggestive of spondyloarthritis (SpA), but do not meet the classification of AS. The goals of treatment are to reduce symptoms, maintain spinal flexibility and normal posture, reduce functional limitations, maintain work ability, and decrease disease complications. The mainstays of treatment have been NSAIDs and exercise, with the additional use of DMARDs in patients with

peripheral arthritis. The American College of Rheumatology (ACR), Spondylitis Association of America (SAA), and Spondyloarthritis Research and Treatment Network (SPARTAN) recommendation for nr-axSpA are the same as AS:

- Stable SpA: conditional recommendation for on-demand treatment with NSAIDs
- Active SpA:
  - First line therapy with continuous NSAIDs with physical therapy
  - TNF inhibitor conditionally recommended for patients with active SpA despite an adequate trial with NSAIDs
    - Lack of response (or intolerance) to at least 2 different NSAIDs over 1 month or incomplete response to at least 2 different NSAIDs over 2 months would be an adequate NSAID trial to judge response
  - TNF-inhibitors are conditionally recommended over secukinumab or ixekizumab
  - Secukinumab or ixekizumab are conditionally recommended over DMARDs in patients that have failed NSAIDs and have contraindications to TNF-inhibitors
  - Recommendations for nonresponse to TNF therapy (all conditional):
    - Primary nonresponse: switch to secukinumab or ixekizumab over another TNF
    - Secondary nonresponse: switch to another TNF over a non-TNF biologic
    - Recommend against addition of sulfasalazine or MTX
    - Recommend against switching to a biosimilar of the failed TNF
  - DMARDs (i.e., methotrexate, sulfasalazine) are only conditionally recommended in patients that have failed NSAIDs and have contraindications to TNF-inhibitors
  - Methotrexate is not recommended as add on therapy to TNF inhibitors in stable and active AS
  - If patient has concomitant inflammatory bowel disease or recurrent uveitis, TNF-inhibitors are recommended over other biologics
  - Glucocorticoids are not recommended

Rheumatoid arthritis (RA)

Rheumatoid arthritis (RA) is the most common inflammatory autoimmune arthritis in adults. The main goal of therapy is to achieve remission, but additional goals include decrease inflammation, relieve symptoms, prevent joint and organ damage, improve physical function/overall well-being, and reduce long term complications.[18,25] The choice of therapy depends on several factors, including the severity of disease activity when therapy is initiated and the response of the patient to prior therapeutic interventions.[18]

American College of Rheumatology (ACR) guidelines list the following guiding principles in the treatment of RA:[18]

- RA requires early evaluation, diagnosis, and management
- Treatment decisions should follow a shared decision-making process
- Treatment decisions should be reevaluated within a minimum of 3 months based on efficacy and tolerability of the DMARD(s) chosen
- Recommendations are limited to DMARDs approved by the US FDA for treatment of RA:
  - csDMARDs: hydroxychloroquine, sulfasalazine, methotrexate (MTX), leflunomide
  - bDMARDs: TNF inhibitors (etanercept, adalimumab, infliximab, golimumab, certolizumab pegol), T cell costimulatory inhibitor (abatacept), IL-6 receptor inhibitors (tocilizumab, sarilumab), anti-CD20 antibody (rituximab)
  - tsDMARDs: JAK inhibitors (tofacitinib, baricitinib, upadacitinib)
- Triple therapy refers to hydroxychloroquine, sulfasalazine, and either methotrexate or leflunomide
- Biosimilars are considered equivalent to FDA-approved originator bDMARDs
- Recommendations referring to bDMARDs exclude rituximab unless patients have had an inadequate response to TNF inhibitors (in order to be consistent with FDA approval) or have a history of lymphoproliferative disorder for which rituximab is an approved therapy

- Treat-to-target refers to a systematic approach involving frequent monitoring of disease activity using validated instruments and modifications of treatment to minimize disease activity with the goal of reaching a predefined target (low disease activity or remission)

ACR guidelines are broken down by previous treatment and disease activity:[18]

- DMARD-naïve patients with moderate-to-high disease activity initial treatment:
  - MTX monotherapy is strongly recommended over hydroxychloroquine, sulfasalazine, bDMARDs monotherapy, tsDMARD monotherapy, or combination of MTX plus a non-TNF bDMARD or tsDMARD
  - MTX monotherapy is conditionally recommended over leflunomide, dual or triple csDMARD therapy, or combination MTX plus a TNF inhibitor
- DMARD-naïve patients with low disease activity initial treatment:
  - Hydroxychloroquine is conditionally recommended over other csDMARDs
  - Sulfasalazine is conditionally recommended over MTX
  - MTX is conditionally recommended over leflunomide
- Initial therapy in csDMARD-treated patients, but MTX naïve, with moderate-to high disease activity:
  - MTX monotherapy is conditionally recommended over combination MTX and a bDMARD or tsDMARD
- Treatment Modifications in patients treated with DMARDs who are not at target:
  - Addition of a bDMARD or tsDMARD is conditionally recommended over triple therapy for patients taking maximally tolerated doses of MTX who are not at target
  - Switching to a bDMARD or tsDMARD of a different class is conditionally recommended over switching to a bDMARD or tsDMARD belonging to the same class for patients taking a bDMARD or tsDMARD who are not at target

Early use of DMARD, particularly MTX, is recommended as soon as possible following diagnosis of RA. Dosing of MTX for RA is once weekly dosing with starting doses at 7.5 mg or 15 mg once weekly.[26-28] MTX dose is increased as tolerated and as needed to control symptoms and signs of RA disease. The usual target dose is at least 15 mg weekly and the usual maximum dose is 25 mg weekly.[27,28] ACR defines optimal dosing for RA treatments as 1) dosing to achieve a therapeutic target derived from mutual patient-clinician consideration of patient priorities and 2) given for at least 3 months before therapy escalation or switching. For patients who are unable to take MTX, hydroxychloroquine, sulfasalazine, or leflunomide are other DMARD options. In patients resistant to initial MTX treatment, combination DMARD (e.g., MTX plus sulfasalazine or hydroxychloroquine or a TNF-inhibitor) is recommended.[18]

For patients who are resistant to MTX after 3 months of treatment at optimal doses (usually 25 mg per week), it is recommended to either use DMARD triple therapy with MTX plus sulfasalazine and hydroxychloroquine or combination of MTX with TNF inhibitor. Triple therapy regimen has been found to be of similar clinical efficacy to MTX with biologics in several randomized trials, including in patients with high level of disease activity or with adverse prognostic features. The use of triple therapy has been shown to be highly cost-effective compared with combining a biologic with MTX, providing comparable or near comparable clinical benefit. The use of biologic with MTX combination is preferred when patients have high disease activity and clinical benefit from a more rapid response is needed and when patients who do not achieve satisfactory response within 3 months with non-biologic triple therapy following an inadequate response to MTX therapy.[18,28]

Polyarticular Juvenile Idiopathic Arthritis (PJIA)[34,35]

Juvenile idiopathic arthritis (JIA) is arthritis that begins before the 16th birthday and persists for at least 6 weeks with other known conditions excluded. Polyarticular juvenile idiopathic arthritis (PJIA) is a subset of JIA. The ACR defines PJIA as arthritis in more than 4 joints during their disease course and excludes systemic JIA. Treatment goals are aimed at achieving clinically inactive

disease and to prevent long-term morbidities, including growth disturbances, joint contractures and destruction, functional limitations, and blindness or visual impairment from chronic uveitis.

The ACR 2019 guidelines recommend the following treatment approach for PJIA:

- NSAIDs are conditionally recommended as adjunct therapy
- DMARD therapy:
  - Methotrexate (MTX) is conditionally recommended over leflunomide and sulfasalazine
  - Subcutaneous MTX is conditionally recommended over oral MTX
- Intraarticular glucocorticoids are conditionally recommended as adjunct therapy and conditionally recommended for bridging only in patients with moderate to high disease activity
- Strongly recommend against chronic low-dose glucocorticoid use, irrespective of disease activity and/or risk factors
- Strongly recommend combination use of a DMARD and infliximab
- Initial therapy for all patients:
  - DMARD is strongly recommended over NSAID monotherapy
  - MTX monotherapy is conditionally recommended over triple DMARD therapy
  - DMARD is conditionally recommended over a biologic
  - Initial biologic therapy may be considered for patients with risk factors and involvement of high-risk joints (e.g., cervical spine, wrist, hip), high disease activity, and/or those judged by their physician to be at high risk of disabling joint damage
- Subsequent therapy:
  - Low disease activity:
    - Escalating therapy (e.g., intraarticular glucocorticoid injections, optimization of DMARD dose, trial of MTX if not already done, and adding or changing biologic agent)
  - Moderate to high disease activity:
    - Add a biologic to original DMARD over changing to a second DMARD or changing to triple DMARD therapy
    - Switch to a non-TNF biologic if currently treated with first TNF ± DMARD over switching to another TNF (unless the patient had good initial response to first TNF)
    - TNF, abatacept, or tocilizumab (depending on prior biologics received) over rituximab after trial of second biologic

Systemic Juvenile Idiopathic Arthritis (SJIA)[19]

Systemic juvenile idiopathic arthritis (SJIA) is a subset of JIA. The ACR defines SJIA as arthritis in greater than or equal to 1 joint for at least 6 weeks' duration in a child less than 16 years of age, with or preceded by a fever of at least 2 weeks' duration that is documented to be daily ("quotidian") for at least 3 days, and accompanied by one or more of the following: evanescent erythematous rash, generalized lymphadenopathy, hepatomegaly or splenomegaly, and serositis. Goals of therapy for SJIA includes control of active inflammation and symptoms, and the prevention of a number of disease and/or treatment related morbidities, such as growth disturbances, joint damage, and functional limitations.

SJIA treatment depends on the presence of active systemic features and physician global assessment score (MD global) and active joint count (AJC):

- Active systemic features and varying degrees of synovitis:
  - Initial therapy: anakinra, glucocorticoids (oral or IV) monotherapy, or NSAID monotherapy
  - Continued disease activity despite initial therapy:
    - 1 month of anakinra: canakinumab, tocilizumab, MTX, leflunomide, or TNF inhibitor
    - 2 weeks of glucocorticoids (GC): anakinra, canakinumab, tocilizumab, MTX, or leflunomide

        - 1 month of NSAIDs: GC monotherapy, anakinra, canakinumab, or tocilizumab
- Without active systemic features and varying degrees of synovitis:
    - Initial therapy: MTX, leflunomide, NSAID monotherapy, or intra-articular GC
    - Continued disease activity despite initial therapy:
        - 3 months of MTX or leflunomide: abatacept, anakinra, TNF inhibitor, or tocilizumab
        - 1 month of NSAIDs: anakinra, MTX, or leflunomide
        - Following initial intra-articular GC joint injection: anakinra, MTX, or leflunomide
    - Continued disease activity despite second line therapy:
        - 1 month of anakinra: abatacept, MTX, leflunomide, TNF inhibitor, or tocilizumab
        - 3 months of MTX or leflunomide: abatacept, anakinra, TNF inhibitor, or tocilizumab

Enthesitis Related Arthritis
Juvenile idiopathic arthritis (JIA) is a group of heterogenous forms of arthritis characterized by onset before 16 years of age, involving one or more joints, and lasting 6 weeks or more. Enthesitis related arthritis (ERA) is one form of JIA in which patients have predominately enthesitis, enthesitis and arthritis, juvenile ankylosing spondylitis, or inflammatory bowel disease associated arthropathy. The International League Against Rheumatism as arthritis and enthesitis that lasts at least 6 weeks in a child less than 16 years OR arthritis or enthesitis with two of the following features: sacroiliac tenderness or inflammatory spinal pain, HLA-B27 positivity, onset of arthritis in a male patient older than 6 years, and family history of HLA-B27 associated disease. Enthesitis is a distinct feature of ERA and is defined as inflammation of an enthesis, which is a site where a tendon, ligament, or joint capsule attaches to bone. (55)

The ACR 2019 guidelines recommend the following treatment approach for ERA:
- NSAIDs are strongly recommended over no treatment in children and adolescents (34)
- TNF inhibitors are conditionally recommended over methotrexate or sulfasalazine in children and adolescents with active enthesitis despite treatment with NSAIDs (34)
- First line therapy with continuous NSAIDs and physical therapy for adult patients (47)
- DMARDs (i.e., methotrexate [MTX], sulfasalazine) are only conditionally recommended in patients that have failed NSAIDs and have contraindications to TNF-inhibitors (47)
    - Lack of response (or intolerance) to at least 2 different NSAIDs over 1 month or incomplete response to at least 2 different NSAIDs over 2 months would be an adequate NSAID trial to judge response (17)

Psoriatic Arthritis (PsA)
Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease associated with psoriasis, most commonly presenting with peripheral arthritis, dactylitis, enthesitis, and spondylitis. Treatment involves the use of a variety of interventions, including many agents used for the treatment of other inflammatory arthritis, particularly spondyloarthritis and RA, and other management strategies of the cutaneous manifestations of psoriasis.[29]

The American Academy of Dermatology (AAD) recommends initiating MTX in most patients with moderate to severe PsA. After 12 to 16 weeks of MTX therapy with appropriate dose escalation, the AAD recommends adding or switching to a TNF inhibitor if there is minimal improvement on MTX monotherapy.[30]

The American College of Rheumatology (ACR) and the National Psoriasis Foundation (NPF) guidelines for PsA recommend a treat-to-target approach in therapy, regardless of disease activity, and the following:[29]
- Active PsA is defined as symptoms at an unacceptably bothersome level as reported by the patient and health care provider to be due to PsA based on the presence of one of the following:
    - Actively inflamed joints

    - Dactylitis
    - Enthesitis
    - Axial disease
    - Active skin and/or nail involvement
    - Extraarticular manifestations such as uveitis or inflammatory bowel disease
- Disease severity includes level of disease activity at a given time point and the presence/absence of poor prognostic factors and long-term damage
- Severe PsA disease includes the presence of 1 or more of the following:
    - Erosive disease
    - Elevated markers of inflammation (ESR, CRP) attributable to PsA
    - Long-term damage that interferes with function (i.e., joint deformities)
    - Highly active disease that causes a major impairment in quality of life
    - Active PsA at many sites including dactylitis, enthesitis
    - Function limiting PsA at a few sites
    - Rapidly progressive disease
- Symptomatic treatments include nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, local glucocorticoid injections
- Treatment recommendations for active disease:
    - Treatment naïve patients first line options include oral small molecules (OSM), TNF biologics, IL-17 inhibitor, and IL-12/23 inhibitor
        - OSM (i.e., methotrexate [MTX], sulfasalazine, cyclosporine, leflunomide, apremilast) should be considered if the patient does not have severe PsA, does not have severe psoriasis, prefers oral therapy, has concern over starting a biologic, or has contraindications to TNF inhibitor
        - Biologics (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor) are recommended as a first line option in patients with severe PsA and/or severe psoriasis
    - Previous treatment with OSM and continued active disease:
        - Switch to a different OSM (except apremilast) in patients without severe PsA or severe PS, contraindications to TNF biologics, prefers oral therapy OR add on apremilast to current OSM therapy
        - May add another OSM (except apremilast) to current OSM therapy for patients that have exhibited partial response to current OSM in patients without severe PsA or severe PS, contraindications to TNF biologics, or prefers oral therapy
        - Biologic (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor) monotherapy
    - Previous treatment with a biologic (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor) and continued active disease:
        - Switch to another biologic (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor, abatacept, or tofacitinib) monotherapy or add MTX to the current TNF biologic

DERMATOLOGICAL DISORDERS

Psoriasis (PS)

Psoriasis (PS) is a chronic inflammatory skin condition that is often associated with systemic manifestations, especially arthritis. Diagnosis is usually clinical, based on the presence of typical erythematous scaly patches, papules, and plaques that are often pruritic and sometimes painful. Treatment goals for psoriasis include improvement of skin, nail, and joint lesions plus enhanced quality of life. [20]

The American Academy of Family Physicians (AAFP) categorizes psoriasis severity into mild to moderate (less than 5% of body surface area [BSA]) and moderate to severe (5% or more of BSA). The AAFP psoriasis treatment guidelines recommend basing treatment on disease severity: [20]

- Mild to moderate (less than 5% of BSA and sparing the genitals, hands, feet, and face):
    - Candidate for intermittent therapy: topical corticosteroids, vitamin D analogs

(calcipotriene and calcitriol), or tazarotene (Tazorac)
    - Candidate for continuous therapy: calcineurin inhibitors (tacrolimus and pimecrolimus)
- Severe (5% or more of BSA or involving the genitals, hands, feet, and face):
    - Less than 20% of BSA affected: vitamin D analogs (calcipotriene and calcitriol) with or without phototherapy. These agents have a slower onset of action but a longer disease-free interval than topical corticosteroids
    - 20% or more of BSA affected: systemic therapy with MTX, cyclosporine, acitretin, or biologics. Biologics are recommended for those with concomitant PsA
- Less commonly used topical therapies include non-medicated moisturizers, salicylic acid, coal tar, and anthralin

The American Academy of Dermatology (AAD) and National Psoriasis Foundation (NPF) categorize psoriasis severity as limited or mild (less than 3% of BSA), moderate (3% to 10% of BSA), or severe (great than 10% of BSA). The AAD/NPF guidelines also note that psoriasis can be considered severe irrespective of BSA when is occurs in select locations (e.g., hands, feet, scalp, face, or genital area) or when it causes intractable pruritus.[31] The AAD psoriasis treatment guidelines recommend the following:[30,33]

- Limited disease (less than 5% of BSA):
    - Topical corticosteroids are first line as either monotherapy or in conjunction with non-steroidal topical agents
    - Vitamin D analogs, calcipotriene, calcipotriol, and calcitriol, are other first line agents and are often used in combination with topical corticosteroids
    - Tazarotene is a corticosteroid sparing agent and can be used in combination with topical corticosteroids to produce a synergistic effect and longer durations of treatment benefit and remission
    - Phototherapy is another first line option for limited disease, and allows for selective targeting of localized lesions and resistant areas such as the scalp and skin folds, leaving surrounding, non-lesional skin unaffected
    - Calcineurin inhibitors (tacrolimus and pimecrolimus) may also be considered first line for intertriginous, inverse, face, and genital psoriasis
    - Systemic agents are considered second line and only for short term use
- Moderate to severe disease without PsA (more than 5% of BSA or psoriasis in vulnerable areas [e.g., face, genitals, hands, and feet] that adversely affects quality of life):
    - UV-therapy is considered first line as monotherapy or in combination with acitretin or MTX
    - If UV-therapy is unavailable, first line therapies include MTX, cyclosporine, acitretin, and biologics
    - Second line systemic agents include leflunomide, sulfasalazine, and tacrolimus
- Biologics are routinely used when one or more traditional systemic agents fail to produce adequate response, but are considered first line in patients with moderate to severe psoriasis with concomitant severe PsA

The National Psoriasis Foundation (NPF) medical board recommend a treat-to-target approach to therapy for psoriasis that include the following:[32]

- The preferred assessment instrument for determining disease severity is BSA
- Target response after treatment initiation should be BSA ≤1% after 3 months
- Acceptable response is either a BSA ≤3% or a BSA improvement ≥75% from baseline at 3 months after treatment initiation

Hidradenitis Suppurativa (HS)[45,46]

Hidradenitis suppurativa (HS) is a chronic inflammatory disease causing painful, nodules to form in the folds of the skin and often secrete puss and blood. HS can be described as mild (single or few lesions in one area of the skin, Hurley Stage I), moderate (repeated cycles of enlarged lesions that

break open and occur in more than one area of the skin, Hurley Stage II), and severe (widespread lesions, scarring, and chronic pain; Hurley Stage III).

Pharmacological treatment for mild HS includes topical clindamycin, oral tetracyclines, hormonal treatment, retinoids, intralesional corticosteroid injections (i.e., triamcinolone), and deroofing. Oral tetracyclines are recommended for mild to moderate HS for at least a 12 weeks course or as long-term maintenance. Combination clindamycin and rifampin is effective second-line therapy for mild to moderate HS, or as first-line or adjunct therapy for severe HS. Combination rifampin, moxifloxacin, and metronidazole are recommended as second or third-line therapy for moderate to severe disease. Dapsone may be effective for a minority of patients with mild to moderate HS as long-term maintenance therapy. Oral retinoids, such as acitretin and isotretinoin, have also been used for mild HS as second or third-line therapy. Hormonal therapy may be considered in female patients for mild to moderate disease as monotherapy, or as adjunct therapy for severe disease. such as hormonal contraceptives, metformin, finasteride, and spironolactone.

Treatment recommendations for moderate to severe and refractory HS include immunosuppressants (e.g., cyclosporine and low dose systemic corticosteroids) and biologic agents. The TNF-inhibitors that are recommended are adalimumab, at doses within FDA labeling, and infliximab, but optimal doses have not been established. Anakinra and ustekinumab may be effective, but require dose ranging studies to determine optimal doses for management.

Atopic Dermatitis

Atopic dermatitis (AD), also known as atopic eczema, is a chronic, pruritic inflammatory dermatosis affecting up to 25% of children and 1-5% of adults. AD follows a relapsing course and is associated with elevated serum immunoglobulin (IgE) levels and a personal or family history of type I allergies, allergic rhinitis, and/or asthma. Onset is most common between 3 and 6 months of age, with approximately 60% of patients developing the eruption in the first year of life and 90% by age 5. While the majority of affected individuals have resolution of disease by adulthood, 10 to 30% do not, and a smaller percentage first develop symptoms as adults. AD has a complex pathogenesis involving genetic, immunologic, and environmental factors, which lead to a dysfunctional skin barrier and dysregulation of the immune system. Clinical findings include erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and lichenification. These clinical findings vary by patient age and chronicity of lesions. Pruritus is a hallmark of the condition that is responsible for much of the disease burden borne by patients and their families. Typical patterns include facial, neck and extensor involvement in infants and children; flexure involvement in any age group, with sparing of groin and axillary regions.[56]

Goals of treatment are to reduce symptoms (pruritus and dermatitis), prevent exacerbations, and minimize therapeutics risks.[60] Despite its relapsing and remitting nature, the majority of patients with AD can achieve clinical improvement and disease control with nonpharmacological interventions (e.g., emollient use), conventional topical therapies (including corticosteroids and calcineurin inhibitors) and environmental and occupational modifications, when necessary.[58-60] The American Academy of Dermatology (AAD) guidelines suggest application of moisturizers should be an integral part of the treatment of patients with AD as there is strong evidence that their use reduces disease severity and need for pharmacologic intervention. They are an important component of maintenance treatment and prevention of flares.[58] The AAD recommends topical corticosteroids (TCS) for patients who fail to respond to good skin care and regular use of emollients alone. Proactive, intermittent use of topical corticosteroids as maintenance therapy (1-2 times weekly) on areas that commonly flare is recommended to help prevent relapses and is more effective than use of emollients alone. Monitoring by physical exam for cutaneous side effects during long-term, potent steroid use is suggested. Proactive, once to twice weekly application of mid-potency TCS for up to 40 weeks has not demonstrated adverse events (e.g., purpura, telangiectasia, striae, focal hypertrichosis, acneiform/rosacea-like eruptions, skin atrophy) in

clinical trials.[58] It is recommended that patients with acute flares use super high or high potency topical corticosteroids for one to two weeks, and then replace these with lower potency preparations until the lesions resolve.[61] AAD notes that mid- to higher potency topical corticosteroids are appropriate for short courses to gain rapid control of symptoms, but long-term management should use the least-potent corticosteroid that is effective.[58] In general, if AD is not responding after 2 weeks of treatment, evaluation to determine other treatment plans is indicated.[57,61]

Topical calcineurin inhibitors (TCIs) (e.g., pimecrolimus, tacrolimus) are recommended by the AAD as second-line therapy and are effective for acute and chronic treatment. They are particularly useful in selected clinical situations such as recalcitrance to steroids; for sensitive areas (face, anogenital, skin folds); for steroid-induced atrophy; and when there is long-term uninterrupted topical steroid use. TCIs are recommended for use on actively affected areas as a steroid-sparing agent. Proactive, intermittent use of TCIs as maintenance therapy (2-3 times per week) on areas that commonly flare is recommended to help prevent relapses while reducing need for topical corticosteroids and is more effective than use of emollients alone.[58] Prescribing information for Elidel® (pimecrolimus) cream and Protopic® (tacrolimus) ointment indicate evaluation after 6 weeks if symptoms of AD do not improve for adults and pediatrics.[62,63]

Phototherapy is recommended as a treatment for both acute and chronic AD in children and adults, after failure of the mentioned above. Systemic immunomodulator agents are indicated and recommended for the subset of adult and pediatric patients in whom optimized topical regimens using emollients, topical anti-inflammatory therapies, adjunctive methods, and/or phototherapy do not adequately control the signs and symptoms of disease. Photo therapy and systemic immunomodulating agents may also be used in patients whose medical, physical, and/or psychological states are greatly affected by their skin disease. Oral cyclosporine, azathioprine, methotrexate, and mycophenolate mofetil are the most commonly used systemic immunomodulators and most efficacious for treating AD. The AAD recommends that systemic corticosteroids should be avoided if possible and should exclusively be reserved for acute, severe exacerbations and as a short-term bridge to other systemic, steroid sparing therapies.[59,64]

INFLAMMATORY BOWEL DISEASE

Crohn's Disease (CD)

Crohn's Disease (CD) is an inflammatory condition that can affect any portion of the gastrointestinal tract from the mouth to the perianal area. Choice of therapy is dependent on the anatomic location of disease, the severity of disease, and whether the treatment goal is to induce remission or maintain remission.[21,36] The American Gastroenterological Association (AGA) 2021 guideline recommends the following:[21]

- Biologic therapy:
  - The AGA suggest early introduction with a biologic, with or without an immunomodulator, rather than delaying their use until after failure of 5-aminosalicylates and/or corticosteroids
  - Anti-TNF (i.e., infliximab or adalimumab) and ustekinumab are recommended over no treatment for the induction and maintenance of remission
  - Vedolizumab is suggested over no treatment for the induction and maintenance of remission
  - AGA suggests against the use of natalizumab over no treatment for the induction and maintenance of remission
  - Patients naïve to biologic therapy, the AGA recommends infliximab, adalimumab, or ustekinumab over certolizumab pegol and suggests the use of vedolizumab over certolizumab pegol for the induction of remission

- Patients with primary non-response to anti-TNF, the AGA recommends ustekinumab and suggests vedolizumab for induction of remission
- Patients with secondary non-response to infliximab, the AGA recommends use of adalimumab or ustekinumab and suggests the use of vedolizumab for the induction of remission (if adalimumab was the first line drug, there is indirect evidence to suggest using infliximab as a second-line agent)

- DMARD therapy:
  - Corticosteroids are suggested over no treatment for the induction of remission, and are recommended against for maintenance of remission
  - Patients in corticosteroid induced remission or with quiescent moderate to severe CD, the AGA suggests thiopurines for maintenance of remission
  - Subcutaneous or intramuscular methotrexate are suggested over no treatment for the induction and maintenance of remission
  - The AGA recommends against the use of 5-aminosalicylates or sulfasalazine over no treatment for the induction or maintenance of remission
  - The AGA suggests against the use of thiopurines over no treatment for achieving remission and recommends biologic drug monotherapy over thiopurine monotherapy for induction of remission
  - The AGA suggests against the use of oral methotrexate monotherapy over no treatment for the induction and maintenance of remission

- Combination therapy:
  - Patients that are naïve to biologics and immunomodulators, the AGA suggest use of infliximab in combination with thiopurines over infliximab monotherapy for the induction and maintenance of remission (combination infliximab with methotrexate may be more effective over infliximab monotherapy)
  - Patients that are naïve to biologics and immunomodulators, the AGA suggest use of adalimumab in combination with thiopurines over adalimumab monotherapy for the induction and maintenance of remission (combination adalimumab with methotrexate may be more effective over adalimumab monotherapy)
  - No recommendations are being made regarding the use of ustekinumab or vedolizumab in combination with thiopurines or methotrexate over biologic monotherapy for induction or maintenance or remission

The 2018 American College of Gastroenterology (ACG) guideline recommends the following[36]:
- Mild to moderately severe disease/low risk disease:
  - Sulfasalazine (in doses of 3-6 grams daily) is effective in colonic and/or ileocolonic CD, but not those with isolated small bowel disease
  - 5-aminosalicylic (ASA) suppositories and enema preparations are effective for induction and maintenance of remission in rectal and sigmoid disease
  - Conventional corticosteroids are primarily used for the treatment of flares, and are often used as a bridge until immunomodulators and/or biologic agents become effective
  - Controlled ileal release budesonide is effective for induction of remission in ileocecal disease
- Moderate to severe disease/moderate to high-risk disease
  - Corticosteroids are effective for short-term use in alleviating signs and symptoms of moderate to severely active CD, but do not induce mucosal healing and should be used sparingly
  - Azathioprine, 6-mercaptopurine, or MTX (15 mg once weekly) may be used in treatment of active disease and as adjunctive therapy for reducing immunogenicity against biologic therapy

    - TNF inhibitors should be used to treat CD that is resistant to treatment with corticosteroids and that is refractory to thiopurines or MTX
    - Vedolizumab with or without an immunomodulator should be considered for induction of symptomatic remission for patients with moderate to severely active CD and objective evidence of active disease
    - Ustekinumab should be used in patients that have failed previous treatment with corticosteroids, thiopurines, MTX, or TNF inhibitors, or in patients with no prior TNF inhibitor exposure
- Severe/fulminant disease:
    - IV corticosteroids should be used
    - TNF inhibitors can be considered
- Maintenance therapy:
    - Thiopurines or methotrexate should be considered once remission is induced with corticosteroids
    - TNF inhibitors, specifically infliximab, adalimumab, and certolizumab pegol, should be used in combination with azathioprine, MTX, or 6-mercaptopurine to maintain remission of TNF induced remission
    - Vedolizumab should be used for maintenance of remission of vedolizumab induced remission
    - Ustekinumab should be used for maintenance of remission of ustekinumab induced remission

Ulcerative Colitis (UC)
Ulcerative colitis (UC) is a chronic immune-mediated inflammatory condition affecting the large intestine associated with inflammation of the rectum, but that can extend to involve additional areas of the colon. The American College of Gastroenterology (ACG) recommends a treat-to-target approach and recommend therapeutic management should be guided by diagnosis (i.e., Montreal classification), assessment of disease activity (i.e., mild, moderate, and severe), and disease prognosis. The ACG treatment recommendations are further broken down into induction therapies and maintenance of remission. The 2019 ACG treatment guidelines recommend the following for therapeutic management of UC[37]:

Induction of remission:
- Mildly active disease:
    - Rectal 5-ASA at a dose of 1 g/day with or without oral 5-ASA at a dose of at least 2 g/day for left-sided UC
    - Rectal 5-ASA at a dose of 1 g/day for ulcerative proctitis
    - Oral 5-ASA at a dose of at least 2 g/day for extensive UC
    - Add oral budesonide multi-matrix (MMX) 9 mg/day for patients that are intolerant or non-responsive to oral and/or rectal and oral 5-ASA at appropriate doses
- Moderately active disease:
    - Oral budesonide multi-matrix (MMX) 9 mg/day for induction of remission
- Moderately to severely active disease:
    - Oral systemic corticosteroids, TNF inhibitors (i.e., adalimumab, golimumab, or infliximab), tofacitinib, or vedolizumab to induce remission
    - Combination of infliximab with thiopurine therapy when using infliximab for induction
    - Switch to tofacitinib or vedolizumab for induction in patients that have failed TNF inhibitors
    - Patients with initial response to TNF inhibitors that lose response should have antibody levels and serum drug levels tested to assess reason for loss of response. If serum levels are adequate, use of another TNF inhibitor is not likely to be of benefit.

Maintenance of remission:

- Previously mildly active disease:
  - Rectal 5-ASA at a dose of 1 g/day in patients with ulcerative proctitis
  - Oral 5-ASA at a dose of at least 2 g/day in patients with left-sided or extensive UC
- Previously moderately to severely active disease:
  - Thiopurines in patients that achieved remission due to corticosteroid induction
  - Continue TNF inhibitors (i.e., adalimumab, golimumab, or infliximab) for remission due to TNF induction
  - Continue vedolizumab for remission due to vedolizumab induction
  - Continue tofacitinib for remission due to tofacitinib induction

The American Gastroenterology Association (AGA) published recommendations for the management of mild to moderate UC[38]:
- Use either standard-dose mesalamine (2-3 g/day) or diazo-bonded 5-ASA for patients with extensive UC for induction of remission and maintenance of remission
- May add rectal mesalamine to oral 5-ASA in patients with extensive or left-sided UC for induction of remission and maintenance of remission
- Use high dose mesalamine (>3 g/day) with rectal mesalamine in patients with suboptimal response to standard-dose mesalamine, diazo-bonded 5-ASA, or with moderate disease activity for induction of remission and maintenance of remission
- Add either oral prednisone or budesonide MMX in patients that are refractory to optimized oral and rectal 5-ASA regardless of disease extent

The American Gastroenterology Association (AGA) published recommendations for the management of moderate to severe UC[48]:
- Standard of care is to continue agents initiated for induction therapy as maintenance therapy, if they are effective (excluding corticosteroids and cyclosporine)
- Adult outpatients with moderate to severe UC:
  - Infliximab, adalimumab, golimumab, vedolizumab, tofacitinib or ustekinumab are strongly recommended over no treatment
  - Biologic naïve patients:
    - infliximab or vedolizumab are conditionally recommended over adalimumab for induction of remission
    - Recommend tofacitinib only be used in the setting of a clinical or registry study
  - Previous exposure to infliximab, particularly those with primary non-response, ustekinumab or tofacitinib are conditionally recommended over vedolizumab or adalimumab for induction of remission
  - Conditionally recommend against use of thiopurine monotherapy for induction, but may be used for maintenance of remission over no treatment

OTHER DISORDERS

Uveitis

Uveitis is inflammation of the uvea, which is the middle layer of the eye, leading to tissue damage and vision loss. There are three types of uveitis: anterior, intermediate and posterior. Uveitis frequently occurs in association with other systemic medical conditions, especially infections and inflammatory disease, but may occur as an isolated process.[39] Treatment of non-infectious uveitis depends on the location of inflammation. Anterior uveitis is generally treated with topical glucocorticoids, such as prednisolone ophthalmic drops.[22,39] Uveitis that is primarily posterior to the lens is generally not responsive to topical medication, although some experts are increasingly using difluprednate.[22] Oral corticosteroids continue to be the mainstay of treatment for noninfectious intermediate, posterior, and pan uveitis. Intraocular and periocular injections of triamcinolone or glucocorticoids are also options, although patients may decline the injections. Systemic treatment is generally reserved for resistant inflammation and may be indicated in patients with glaucoma

who cannot be treated with local injection. If remission has been achieved for 6 to 12 months with systemic glucocorticoids, the maintenance dose may be gradually discontinued.[22,42] The American Academy of Ophthalmology recommends the use of immunosuppressive agents, such as methotrexate, azathioprine, mycophenolate, cyclosporine, and tacrolimus, for patients that are intolerant and/or resistant to systemic corticosteroids. TNF-inhibitors, such as adalimumab, are recommended if the patient is inadequately controlled by corticosteroids and non-corticosteroid systemic immunomodulatory therapies.[22,42]

Giant Cell Arteritis (GCA)
Giant cell arteritis (GCA), also known as Horton disease, cranial arteritis, and temporal arteritis, is a blood vessel disease that commonly occurs with polymyalgia rheumatica. It is a type of vasculitis involving mostly the arteries of the scalp and head, especially the arteries over the temples. Due to the risk of vision loss, treatment should begin as soon as possible.[23]

The American College of Rheumatology/Vasculitis Foundation guidelines recommend High-dose systemic glucocorticoids as the mainstay of therapy for GCA. The guidelines provide the following recommendations for the medical management of GCA[40]:

- Patients with newly diagnosed active GCA with visual symptoms/loss or critical cranial ischemia:
    - High dose IV pulse corticosteroids followed by high dose oral corticosteroids with or without a non-corticosteroid immunosuppressive agent (i.e., methotrexate or tocilizumab)
    - Taper oral corticosteroids in patients that achieve remission
    - Consider adding on or changing non-corticosteroid immunosuppressive agent in patients that have not achieved remission
- Patients with newly diagnosed active GCA without visual symptoms/loss or critical cranial ischemia:
    - High dose oral corticosteroids with or without a non-corticosteroid immunosuppressive agent (i.e., methotrexate or tocilizumab)
    - Taper oral corticosteroids in patients that achieve remission
    - Consider adding on or changing non-corticosteroid immunosuppressive agent in patients that have not achieved remission

Cryopyrin-Associated Periodic Syndromes (CAPS)/Neonatal-Onset Multisystem Inflammatory Disease[24,41]
Cryopyrin-associated periodic syndrome (CAPS) is a rare autosomal dominant hereditary autoimmune disorder associated with a defect in the cryopyrin protein. CAPS syndrome is caused by a gain of function mutation in the NLRP3 gene leading to over secretion of fever causing cytokine IL-1B.[50] There are three distinct phenotypes related to a defect in the same gene but differ in the organs involved and disease severity. Familial cold autoinflammatory syndrome (FCAS) is the mildest form and more common in the United States. Muckle-Wells syndrome (MWS) is the intermediate phenotype and more common in Europe. Neonatal-onset multisystem inflammatory disease (NOMID) is the least common disease and is the most severe form. An international task force recommends both of the following diagnostic criteria need to be present for a diagnosis CAPS and its subtypes[49]:

- Raised inflammatory markers (CRP/SAA)
- The presence of at least two of the following signs/symptoms:
    - Urticaria-like rash
    - Cold/stress triggered episodes
    - Sensorineural hearing loss
    - Musculoskeletal symptoms of arthralgia/arthritis/myalgia
    - Chronic aseptic meningitis
    - Skeletal abnormalities of epiphyseal overgrowth/frontal bossing

FCAS is characterized by a hive-like rash that is associated with exposure to cold and other environmental triggers and with symptoms lasting up to 24 hours. Patients experience urticaria, arthralgia, fever with chills, severe thirst, red-eyes, and headache after a general cold exposure, including air conditioning. In MWS, inflammation can occur spontaneously as well as from triggers, such as stress, cold, or exercise, with episodes lasting from one to three days. MWS shares the same characteristics as FCAS, but is also characterized by renal amyloidosis, sensorineural hearing loss, and conjunctivitis. Hearing loss, partial or complete, often develop by teenage years.

NOMID is characterized by neonatal onset of cutaneous symptoms along with fever with inflammation in multiple organ systems. NOMID shares most of the same characteristics with FCAS and MWS, but also has more severe arthropathy, chronic urticaria, and CNS involvement. CNS manifestations range from hearing loss to aseptic meningitis and mental disabilities. Arthropathy typically affects the large joints, resulting in joint enlargement and functional disability.

Interleukin (IL)-1-beta inhibitors (e.g., anakinra, rilonacept, and canakinumab) have shown effectiveness in preventing and alleviating symptoms of CAPS and reducing levels of inflammatory indices, including serum amyloid A. Treatment with non-steroidal anti-inflammatory drugs, disease modifying antirheumatic drugs, and glucocorticoids offered only some patients partial symptom control.

Deficiency of the IL-1 Receptor Antagonist (DIRA)
Deficiency of the IL-1 Receptor Antagonist (DIRA) syndrome is a relatively new autoinflammatory disease linked to activation of the IL-1 pathway. The DIRA syndrome is distinct from the cryopyrinopathies by its neonatal onset of sterile multifocal osteomyelitis, periostitis, and neutrophilic pustulosis. DIRA is caused by a loss of function of the endogenous IL-1 receptor antagonist, which results in unopposed proinflammatory signaling via cytokines IL-1alpha and IL-1beta on IL-1 receptor type 1. There has been a common homozygous mutation in the IL1RN gene detected in a number of patients. DIRA has similar cutaneous and systemic features as infantile pustular psoriasis and SAPHO (synovitis, acne, pustulosis, hyperostosis, and osteitis) syndrome. The diagnosis of DIRA can be confirmed via genetic testing.[50] DIRA is extremely responsive to IL-1 blockade and anakinra has been used empirically. The FDA approved anakinra as treatment for DIRA and rilonacept as maintenance therapy once a patient has achieved remission of DIRA.[51]

Systemic Sclerosis (Scleroderma)-Associated Interstitial Lung Disease (ILD)
Systemic sclerosis is a connective tissue disease (CTD) that affects numerous organ systems, including skin, blood vessels, heart, lungs, kidneys, gastrointestinal, and musculoskeletal. Pulmonary disease is the leading cause of death in patients with systemic sclerosis, and ILD is a common manifestation that tends to occur early in the course of systemic sclerosis.[52]

The American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) collaborated on classification criteria for the diagnosis of systemic sclerosis, in which they note that systemic sclerosis-associated ILD is diagnosed when there is radiographic evidence of diffuse parenchymal lung disease in patients with systemic sclerosis. The ACR/EULAR criteria note that ILD is defined as pulmonary fibrosis seen on HRCT or chest radiography, most pronounced in the basilar portions of the lungs.[54]

The American College of Rheumatology (ACR) published a treatment algorithm for systemic sclerosis and related conditions. The ACR recommends the following treatment options for ILD associated with systemic sclerosis:[53]

Induction therapy:
- Mycophenolate mofetil (MMF) as first line therapy

- IV cyclophosphamide as second line therapy
- Rituximab as third line therapy
- Lung transplant or hemopoietic stem cell transplant for select patients as fourth line therapy

Maintenance therapy:
- Mycophenolate mofetil (MMF) as first line therapy
- Azathioprine as second line therapy
- IV or oral cyclophosphamide as third line therapy

Safety[1-16,43,44]

Actemra

Tocilizumab has the following boxed warning:
- Increased risk for developing serious infections that may lead to hospitalization or death, including tuberculosis (TB), bacterial, invasive fungal, viral, and other opportunistic infections. Perform test for latent TB, and if positive, start treatment for TB prior to initiating therapy. Monitor all patients for active TB during treatment, even if initial latent TB test is negative.

Tocilizumab is contraindicated in patients with a known hypersensitivity reaction to tocilizumab.

Cimzia

Certolizumab has the following boxed warnings:
- Increased risk for developing serious infections that may lead to hospitalization or death, including tuberculosis (TB), bacterial, invasive fungal, viral, and other opportunistic infections. Perform test for latent TB, and if positive, start treatment for TB prior to initiating therapy. Monitor all patients for active TB during treatment, even if initial latent TB test is negative.
- Lymphoma and other malignancies, some fatal have been reported in children and adolescent patients treated with TNF blockers. Cimzia is not indicated for use in pediatric patients.

Certolizumab is contraindicated in patients with a severe hypersensitivity to certolizumab pegol or to any of the excipients.

Cosentyx

Secukinumab is contraindicated in patients with a serious hypersensitivity reaction to secukinumab or to any of the excipients.

Enbrel

Etanercept has the following boxed warnings:
- Increased risk for developing serious infections that may lead to hospitalization or death, including tuberculosis (TB), bacterial, invasive fungal, viral, and other opportunistic infections. Perform test for latent TB, and if positive, start treatment for TB prior to initiating therapy. Monitor all patients for active TB during treatment, even if initial latent TB test is negative.
- Lymphoma and other malignancies, some fatal have been reported in children and adolescent patients treated with TNF blockers.

Etanercept is contraindicated for use in patients with sepsis.

Humira

Adalimumab has the following boxed warnings:

- Increased risk for developing serious infections that may lead to hospitalization or death, including tuberculosis (TB), bacterial, invasive fungal, viral, and other opportunistic infections. Perform test for latent TB, and if positive, start treatment for TB prior to initiating therapy. Monitor all patients for active TB during treatment, even if initial latent TB test is negative.
- Lymphoma and other malignancies, some fatal have been reported in children and adolescent patients treated with TNF blockers.
- Post marketing cases of hepatosplenic T-cell lymphoma have occurred in adolescents and young adults with inflammatory bowel disease treated with TNF blockers

Kevzara
Sarilumab has the following boxed warning:
- Increased risk for developing serious infections that may lead to hospitalization or death, including tuberculosis (TB), bacterial, invasive fungal, viral, and other opportunistic infections. Perform test for latent TB, and if positive, start treatment for TB prior to initiating therapy. Monitor all patients for active TB during treatment, even if initial latent TB test is negative.

Sarilumab is contraindicated in patients with a known hypersensitivity to sarilumab or any of the inactive ingredients.

Kineret
Anakinra is contraindicated in patients with a known hypersensitivity to E.coli-derived proteins, anakinra, or any component of the product.

Olumiant
Baricitinib has the following boxed warnings:
- Increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to hospitalization or death, including tuberculosis (TB). Interrupt treatment with Olumiant if serious infection occurs until the infection is controlled. Test for latent TB before and during therapy, and if positive, start treatment for TB prior to use. Monitor all patients for active TB during treatment, even if initial latent TB test is negative.
- Higher rate of all-cause mortality, including sudden cardiovascular death with another Janus Kinase (JAK) inhibitor vs tumor necrosis factor (TNF) blockers in RA patients
- Malignancies have occurred in patients treated with Olumiant. Higher rate of lymphomas and lung cancers with another JAK inhibitor vs TNF blockers in RA patients
- Higher rate of MACE (defined as cardiovascular death, myocardial infarction, and stroke) with another JAK inhibitor vs TNF blockers in RA patients
- Thrombosis has occurred in patients treated with Olumiant. Increased incidence of pulmonary embolism, venous and arterial thrombosis with another JAK inhibitor vs TNF blockers.

Baricitinib does not have any FDA labeled contraindications for use.

Orencia
Abatacept does not have any FDA labeled contraindications for use.

Rinvoq
Upadacitinib has the following boxed warnings:
- Increased risk of serious bacterial, fungal, viral, and opportunistic infections leading to hospitalization or death, including tuberculosis (TB). Interrupt treatment with Rinvoq if serious infection occurs until the infection is controlled. Test for latent TB before and during

therapy, and if positive, start treatment for TB prior to use. Monitor all patients for active TB during treatment, even if initial latent TB test is negative.
- Higher rate of all-cause mortality, including sudden cardiovascular death with another Janus Kinase (JAK) inhibitor vs tumor necrosis factor (TNF) blockers in RA patients
- Malignancies have occurred in patients treated with Rinvoq. Higher rate of lymphomas and lung cancers with another JAK inhibitor vs TNF blockers in RA patients
- Higher rate of MACE (defined as cardiovascular death, myocardial infarction, and stroke) with another JAK inhibitor vs TNF blockers in RA patients
- Thrombosis has occurred in patients treated with Rinvoq. Increased incidence of pulmonary embolism, venous and arterial thrombosis with another JAK inhibitor vs TNF blockers.

Upadacitinib is contraindicated in patients with known hypersensitivity to upadacitinib or any of its excipients.

Siliq
Brodalumab has the following boxed warning:
- Suicidal ideation and behavior, including completed suicides, have occurred in patients.

Simponi
Golimumab has the following boxed warnings:
- Increased risk for developing serious infections that may lead to hospitalization or death, including tuberculosis (TB), bacterial, invasive fungal, viral, and other opportunistic infections. Perform test for latent TB, and if positive, start treatment for TB prior to initiating therapy. Monitor all patients for active TB during treatment, even if initial latent TB test is negative.
- Lymphoma and other malignancies, some fatal have been reported in children and adolescent patients treated with TNF blockers.

Skyrizi
Risankizumab is contraindicated in patients with a history of serious hypersensitivity reaction to risankizumab-rzaa or any of the excipients.

Stelara
Ustekinumab is contraindicated for use in patients with clinically significant hypersensitivity to ustekinumab or to any of the excipients.

Taltz
Ixekizumab is contraindicated for use in patients with serious hypersensitivity reaction to ixekizumab or to any of the excipients.

Tremfya
Guselkumab is contraindicated for use in patients with serious hypersensitivity reaction to guselkumab or to any of the excipients.

Xeljanz/Xeljanz XR
Tofacitinib has the following boxed warnings:
- Increased risk serious bacterial, fungal, viral, and opportunistic infections leading to hospitalization or death, including tuberculosis (TB). Interrupt treatment with Xeljanz/Xeljanz XR if serious infection occurs until the infection is controlled. Test for latent TB before and during therapy, and if positive, start treatment for TB prior to initiating therapy. Monitor all patients for active TB during treatment, even if initial latent TB test is negative.

- Higher rate of all-cause mortality, including sudden cardiovascular death with Xeljanz vs TNF blockers in RA patients
- Higher rate of MACE (defined as cardiovascular death, myocardial infarction, and stroke) with Xeljanz vs TNF blockers in RA patients.
- Thrombosis has occurred in patients treated with Xeljanz. Increased incidence of pulmonary embolism, venous and arterial thrombosis with Xeljanz vs TNF blockers in RA patients.
- Malignancies have occurred in patients treated with Xeljanz. Higher rate of lymphomas and lung cancers with Xeljanz vs TNF blockers in RA patients.

Tofacitinib does not have any FDA labeled contraindications for use.

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Biologic Immunomodulators Prior Authorization with Quantity Limit

TARGET AGENT(S)
Prerequisite Biologic Immunomodulators (See table below) (NOTE: For Otezla- please see Otezla PA; for Zeposia- please see Zeposia PA)

Actemra® (tocilizumab)
Cimzia® (certolizumab pegol)
Cosentyx® (secukinumab)
Enbrel® (etanercept)
Humira® (adalimumab)
Kevzara® (sarilumab)
Kineret® (anakinra)
Olumiant® (baricitinib)
Orencia® (abatacept)
Rinvoq™ (upadacitinib extended release)
Siliq™ (brodalumab)
Simponi® (golimumab)
Skyrizi™ (risankizumab-rzaa)
Stelara® (ustekinumab)
Taltz® (ixekizumab)
Tremfya® (guselkumab)
Xeljanz® (tofacitinib)
Xeljanz XR® (tofacitinib extended release)

Disease State	Step 1		Step 2 (Directed to ONE step 1 agent)	Step 3a (Directed to TWO step 1 agents)	Step 3b (Directed to TWO agents from step 1 and/or step 2)	Step 3c (Directed to THREE step 1 agents)
	Step 1a	Step 1b (Directed to ONE TNF inhibitor) NOTE: Please see Step 1a for preferred TNF inhibitors				
Rheumatoid Disorders						
Ankylosing Spondylitis (AS)	SQ: Cosentyx, Enbrel, Humira	Oral: Xeljanz, Xeljanz XR	N/A	SQ: Cimzia, Simponi, Taltz	N/A	N/A
Nonradiographic Axial Spondyloarthritis (nr-axSpA)	SQ: Cimzia, Cosentyx	N/A	N/A	SQ: Taltz	N/A	N/A
Polyarticular Juvenile Idiopathic Arthritis (PJIA)	SQ: Enbrel, Humira	Oral: Xeljanz	SQ: Actemra (Humira is required	N/A	SQ: Orencia	N/A

			Step 1 agent)			
Psoriatic Arthritis (PsA)	SQ: Cosentyx, Enbrel, Humira, Skyrizi, Stelara, Tremfya Oral: Otezla	Oral: Rinvoq, Xeljanz, Xeljanz XR	N/A	SQ: Cimzia, Orencia, Simponi, Taltz	N/A	N/A
Rheumatoid Arthritis	SQ: Enbrel, Humira	Oral: Rinvoq, Xeljanz, Xeljanz XR	SQ: Actemra (Humira is required Step 1 agent)	Oral: Olumiant SQ: Cimzia, Kevzara, Kineret, Orencia, Simponi	N/A	N/A
Dermatological Disorder						
Hidradenitis Suppurativa (HS)	SQ: Humira	N/A	N/A	N/A	N/A	N/A
Psoriasis (PS)	SQ: Cosentyx, Enbrel, Humira, Skyrizi, Stelara, Tremfya Oral: Otezla	N/A	N/A	SQ: Cimzia, Ilumya	N/A	SQ: Siliq, Taltz
Inflammatory Bowel Disease						
Crohn's Disease	SQ: Humira, Stelara	N/A	SQ: Cimzia (Humira is required Step 1 agent)	N/A	N/A	N/A
Ulcerative Colitis	SQ: Humira, Stelara	N/A	SQ: Simponi (Humira is required Step 1 agent) Oral: Rinvoq (Humira is required	N/A	Zeposia (Humira, Rinvoq, Stelara, OR Xeljanz/Xeljanz XR are required Step agents)	N/A

			Step 1 agent), Xeljanz, Xeljanz XR			
Other						
Uveitis	SQ: Humira	N/A	N/A	N/A	N/A	N/A
Indications Without Prerequisite Biologic Immunomodulators Required						
Atopic Dermatitis Deficiency of IL-1 Receptor Antagonist (DIRA) Enthesitis Related Arthritis (ERA) Giant Cell Arteritis (GCA) Neonatal-Onset Multisystem Inflammatory Disease (NOMID) Systemic Juvenile Idiopathic Arthritis (SJIA) Systemic Sclerosis-associated Interstitial Lung Disease (SSc-ILD)	N/A	N/A	N/A	N/A	N/A	N/A

*Note: A trial of either or both Xeljanz products (Xeljanz and Xeljanz XR) collectively counts as ONE product

Brand (generic)	GPI	Multisource Code	Quantity Limit (per day or as listed)*
Actemra (tocilizumab)			
162 mg/0.9 mL auto-injector	6650007000D520	M, N, O, or Y	4 pens (3.6 mL)/28 days
162 mg/0.9 mL syringe	6650007000E520	M, N, O, or Y	4 syringes (3.6 mL)/28 days

Brand (generic)	GPI	Multisource Code	Quantity Limit (per day or as listed)*
Cimzia (certolizumab)			
2 x 200 mg/mL syringe kit	5250502010F840	M, N, O, or Y	2 kits/28 days
6 X 200 mg/mL syringe starter kit	52505020106460 5250502010F860	M, N, O, or Y	1 starter kit (3 doses)/180 days
Cosentyx (secukinumab)			
150 mg/mL pen	9025057500D520	M, N, O, or Y	1 pen/28 days
300 mg/2 mL (2 x 150 mg/mL) pen	9025057500D530	M, N, O, or Y	2 pens/28 days
75 mg/0.5 mL syringe	9025057500E510	M, N, O, or Y	1 syringe/28 days
150 mg/mL syringe	9025057500E520	M, N, O, or Y	1 syringe/28 days
300 mg/2 mL (2 x 150 mg/mL) syringe	9025057500E530	M, N, O, or Y	2 syringes/28 days
Enbrel (etanercept)			
25 mg/0.5 mL single use vial	66290030002015	M, N, O, or Y	8 vials (4 mLs)/28 days
25 mg multiple dose vial kit	66290030002120	M, N, O, or Y	8 vials/28 days
50 mg/mL SureClick auto-injector	6629003000D530	M, N, O, or Y	4 pens (4 mL)/28 days
50 mg/mL cartridge	6629003000E230	M, N, O, or Y	4 cartridges (4 mL)/28 days
25 mg/0.5 mL syringe	6629003000E525	M, N, O, or Y	4 syringes (2.04 mL)/28 days
50 mg/mL syringe	6629003000E530	M, N, O, or Y	4 syringes (4 mL)/28 days
Humira (adalimumab)			
10 mg/0.1 mL syringe	6627001500F804	M, N, O, or Y	2 syringes/28 days
10 mg/0.2 mL syringe	6627001500F805	M, N, O, or Y	2 syringes/28 days
20 mg/0.2 mL syringe	6627001500F809	M, N, O, or Y	2 syringes/28 days
20 mg/0.4 mL syringe kit	6627001500F810	M, N, O, or Y	2 syringes/28 days
40 mg/0.8 mL syringe kit	6627001500F820	M, N, O, or Y	2 syringes/28 days
40 mg/0.4 mL syringe	6627001500F830	M, N, O, or Y	2 syringes/28 days
Pediatric Crohn's Disease starter kit 80 mg/0.8 mL syringe	6627001500F840	M, N, O, or Y	1 kit (3 syringes)/180 days
Pediatric Crohn's Disease starter kit 40 mg/0.4 mL and 80 mg/0.8 mL syringe	6627001500F880	M, N, O, or Y	1 kit (2 syringes)/180 days
40 mg/0.8 mL pen	6627001500F420 (NDC 00074433902)	M, N, O, or Y	2 pens/28 days
Psoriasis, Uveitis starter kit 40 mg/0.8 mL pen	6627001500F420 (NDC 00074433907)	M, N, O, or Y	1 kit (4 pens)/180 days
Crohn's Disease, Ulcerative Colitis, or	6627001500F420	M, N, O, or Y	1 kit (6 pens)/180 days

Brand (generic)	GPI	Multisource Code	Quantity Limit (per day or as listed)*
Hidradenitis starter kit 40 mg/0.8 mL pen	(NDC 00074433906)		
40 mg/0.4 mL pen	6627001500F430	M, N, O, or Y	2 pens/28 days
80 mg/0.8 mL pen	6627001500F440 (NDC 00074012402)	M, N, O, or Y	2 pens/28 days
Crohn's Disease, Ulcerative Colitis, or Hidradenitis starter kit 80 mg/0.8 mL pen	6627001500F440 (NDC 00074012403)	M, N, O, or Y	1 kit (3 pens)/180 days
Pediatric Ulcerative Colitis starter kit 80 mg/0.8 mL pen	6627001500F440 (NDC 00074012404)	M, N, O, or Y	1 kit (4 pens)/180 days
Psoriasis, Uveitis starter kit 80 mg/0.8 mL and 40 mg/0.4 mL pen	6627001500F450	M, N, O, or Y	1 kit (3 pens)/180 days
Kevzara (sarilumab)			
150 mg/1.14 mL pen	6650006000D520	M, N, O, or Y	2 pens (2.28 mL)/28 days
200 mg/1.14 mL pen	6650006000D530	M, N, O, or Y	2 pens (2.28 mL)/28 days
150 mg/1.14 mL syringe	6650006000E520	M, N, O, or Y	2 syringes (2.28 mL)/28 days
200 mg/1.14 mL syringe	6650006000E530	M, N, O, or Y	2 syringes (2.28 mL)/28 days
Kineret (anakinra)			
100 mg syringe	6626001000E520	M, N, O, or Y	28 syringes (18.76 mL)/28 days
Olumiant (baricitinib)			
1 mg tablets	66603010000310	M, N, O, or Y	1 tablet/day
2 mg tablets	66603010000320	M, N, O, or Y	1 tablet/day
Orencia (abatacept)			
50 mg/0.4 mL syringe	6640001000E510	M, N, O, or Y	4 syringes (1.6 mL)/28 days
87.5 mg/ 0.7 mL syringe	6640001000E515	M, N, O, or Y	4 syringes (2.8 mL)/28 days
125 mg/mL syringe	6640001000E520	M, N, O, or Y	4 syringes (4 mL)/28 days
125 mg/mL ClickJect auto-injector	6640001000D520	M, N, O, or Y	4 syringes (4 mL)/28 days
Rinvoq (upadacitinib)			
15 mg tablet	66603072007520	M, N, O, or Y	1 tablet/day
30 mg tablet	66603072007530	M, N, O, or Y	1 tablet/day
45 mg tablet	66603072007540	M, N, O, or Y	56 tablets/365 days
Siliq (brodalumab)			
210 mg/1.5 mL syringe	9025052000E520	M, N, O, or Y	2 syringes (3 mL)/28 days
Simponi (golimumab)			
50 mg/0.5 mL auto-injector	6627004000D520	M, N, O, or Y	1 syringe (0.5 mL)/28 days

Brand (generic)	GPI	Multisource Code	Quantity Limit (per day or as listed)*
50 mg/0.5 mL syringe	6627004000E520	M, N, O, or Y	1 syringe (0.5 mL)/28 days
100 mg/1 mL auto-injector	6627004000D540	M, N, O, or Y	1 syringe (1 mL)/28 days
100 mg/1 mL syringe	6627004000E540	M, N, O, or Y	1 syringe (1 mL)/28 days
Skyrizi (risankizumab-rzaa)			
150 mg/mL auto-injector	9025057070D520	M, N, O, or Y	1 pen (1 mL)/84 days
150 mg/mL prefilled syringe	9025057070E540	M, N, O, or Y	1 syringe (1 mL)/84 days
2 x 75 mg/0.83 mL syringe kit	9025057070F820	M, N, O, or Y	1 kit/84 days
Stelara (ustekinumab)			
45 mg/0.5 mL vial	90250585002020	M, N, O, or Y	1 vial (0.5 mL)/84 days
45 mg/0.5 mL syringe	9025058500E520	M, N, O, or Y	1 syringe (0.5 mL)/84 days
90 mg/1 mL syringe	9025058500E540	M, N, O, or Y	1 syringe (1 mL)/56 days
Taltz (ixekizumab)			
80 mg/mL auto-injector	9025055400D520	M, N, O, or Y	1 syringe (1 mL)/28 days
80 mg/mL syringe	9025055400E520	M, N, O, or Y	1 syringe (1 mL)/28 days
Tremfya (guselkumab)			
100 mg/mL pen	9025054200D220	M, N, O, or Y	1 pen (1 mL)/56 days
100 mg/mL syringe	9025054200E520	M, N, O, or Y	1 syringe (1 mL)/56 days
Xeljanz (tofacitinib)			
5 mg tablet	66603065100320	M, N, O, or Y	2 tablets/day
10 mg tablet	66603065100330	M, N, O, or Y	240 tablets/365 days
1 mg/mL oral solution	66603065102020	M, N, O, or Y	240 mL/30 days
Xeljanz XR (tofacitinib extended release)			
11 mg tablet	66603065107530	M, N, O, or Y	1 tablet/day
22 mg tablet	66603065107550	M, N, O, or Y	120 tablets/365 days

* Requested quantities above the listed quantity limits will be approved based on FDA labeled and/or compendia supported doses for the requested indication

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Initial Evaluation
Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
   A. The requested agent is eligible for continuation of therapy AND ONE of the following:
      i. Information has been provided that indicates the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days
      OR

ii. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed

Agents Eligible for Continuation of Therapy
All target agents are eligible for continuation of therapy

OR

B. ALL of the following:
   i. The patient has an FDA labeled indication or an indication supported in compendia for the requested agent and route of administration
   AND
   ii. ONE of the following:
      a. The patient's age is within FDA labeling for the requested indication for the requested agent
      OR
      b. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication
   AND
   iii. ONE of the following:
      a. The patient has a diagnosis of moderately to severely active rheumatoid arthritis (RA) AND BOTH of the following:
         1. ONE of the following:
            i. The patient has tried and had an inadequate response to maximally tolerated methotrexate (e.g., titrated to 25 mg weekly) for at least 3-months
            OR
            ii. The patient has tried and had an inadequate response to another conventional agent (i.e., hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA for at least 3-months
            OR
            iii. The patient has an intolerance or hypersensitivity to ONE of the following conventional agents (i.e., maximally tolerated methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA
            OR
            iv. The patient has an FDA labeled contraindication to ALL of the following conventional agents (i.e., methotrexate, hydroxychloroquine, leflunomide, sulfasalazine) used in the treatment of RA
            OR
            v. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of RA

         AND

         2. If the request is for Simponi, ONE of the following:
            i. The patient will be taking the requested agent in combination with methotrexate
            OR
            ii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to methotrexate

      OR

b. The patient has a diagnosis of active psoriatic arthritis (PsA) AND ONE of the following:
    1. The patient has tried and had an inadequate response to ONE conventional agent (i.e., cyclosporine, leflunomide, methotrexate, sulfasalazine) used in the treatment of PsA for at least 3-months
    OR
    2. The patient has an intolerance or hypersensitivity to ONE of the conventional agents used in the treatment of PsA
    OR
    3. The patient has an FDA labeled contraindication to ALL of the conventional agents used in the treatment of PsA
    OR
    4. The patient has severe active PsA (e.g., erosive disease, elevated markers of inflammation [e.g., ESR, CRP] attributable to PsA, long-term damage that interferes with function [i.e., joint deformities], rapidly progressive)
    OR
    5. The patient has concomitant severe psoriasis (PS) (e.g., greater than 10% body surface area involvement, occurring on select locations [i.e., hands, feet, scalp, face, or genitals], intractable pruritus, serious emotional consequences)
    OR
    6. The patient's medication history indicates use of another biologic immunomodulator agent OR Otezla that is FDA labeled or supported in compendia for the treatment of PsA

OR

c. The patient has a diagnosis of moderate to severe plaque psoriasis (PS) AND ONE of the following:
    1. The patient has tried and had an inadequate response to ONE conventional agent (i.e., acitretin, anthralin, calcipotriene, calcitriol, coal tar products, cyclosporine, methotrexate, pimecrolimus, PUVA [phototherapy], tacrolimus, tazarotene, topical corticosteroids) used in the treatment of PS for at least 3-months
    OR
    2. The patient has an intolerance or hypersensitivity to ONE conventional agent used in the treatment of PS
    OR
    3. The patient has an FDA labeled contraindication to ALL conventional agents used in the treatment of PS
    OR
    4. The patient has severe active PS (e.g., greater than 10% body surface area involvement, occurring on select locations [i.e., hands, feet, scalp, face, or genitals], intractable pruritus, serious emotional consequences)
    OR
    5. The patient has concomitant severe psoriatic arthritis (PsA) (e.g., erosive disease, elevated markers of inflammation [e.g., ESR, CRP] attributable to PsA, long-term damage that interferes with function [i.e., joint deformities], rapidly progressive)
    OR

6. The patient's medication history indicates use of another biologic immunomodulator agent OR Otezla that is FDA labeled or supported in compendia for the treatment of PS

OR

d. The patient has a diagnosis of moderately to severely active Crohn's disease (CD) AND ONE of the following:
    1. The patient has tried and had an inadequate response to ONE conventional agent (i.e., 6-mercaptopurine, azathioprine, corticosteroids [e.g., prednisone, budesonide EC capsule], methotrexate) used in the treatment of CD for at least 3-months
    OR
    2. The patient has an intolerance or hypersensitivity to ONE of the conventional agents used in the treatment of CD
    OR
    3. The patient has an FDA labeled contraindication to ALL of the conventional agents used in the treatment of CD
    OR
    4. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of CD

OR

e. The patient has a diagnosis of moderately to severely active ulcerative colitis (UC) AND ONE of the following:
    1. The patient has tried and had an inadequate response to ONE conventional agent (i.e., 6-mercaptopurine, azathioprine, balsalazide, corticosteroids, cyclosporine, mesalamine, sulfasalazine) used in the treatment of UC for at least 3-months
    OR
    2. The patient has severely active ulcerative colitis
    OR
    3. The patient has an intolerance or hypersensitivity to ONE of the conventional agents used in the treatment of UC
    OR
    4. The patient has an FDA labeled contraindication to ALL of the conventional agents used in the treatment of UC
    OR
    5. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of UC

OR

f. The patient has a diagnosis of non-infectious intermediate uveitis, posterior uveitis, or panuveitis AND ONE of the following:
    1. BOTH of the following:
        i. ONE of the following:
            A. The patient has tried and had an inadequate response to oral corticosteroids used in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis for a minimum of 2 weeks
            OR
            B. The patient has tried and had an inadequate response to periocular or intravitreal

corticosteroid injections in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis

OR

C. The patient has an intolerance or hypersensitivity to oral corticosteroids OR periocular or intravitreal corticosteroid injections used in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis

OR

D. The patient has an FDA labeled contraindication to BOTH oral corticosteroids and periocular/intravitreal corticosteroids

AND

ii. ONE of the following:

A. The patient has tried and had an inadequate response to ONE conventional systemic agent (i.e., azathioprine, mycophenolate, methotrexate, cyclosporine, tacrolimus) used in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis for at least 3-months

OR

B. the patient has an intolerance or hypersensitivity to ONE conventional systemic agent used in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis

OR

C. The patient has an FDA labeled contraindication to ALL conventional systemic agents used in the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis

OR

2. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis

OR

g. The patient has a diagnosis of giant cell arteritis (GCA) AND ONE of the following:

1. The patient has tried and had an inadequate response to systemic corticosteroids (e.g., prednisone, methylprednisolone) used in the treatment of GCA for at least 7-10 days

OR

2. The patient has an intolerance or hypersensitivity to systemic corticosteroids used in the treatment of GCA

OR

3. The patient has an FDA labeled contraindication to ALL systemic corticosteroids

OR

4. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of GCA

OR

h. The patient has a diagnosis of active ankylosing spondylitis (AS) AND ONE of the following:
    1. The patient has tried and had an inadequate response to two different NSAIDs used in the treatment of AS for at least a 4-week total trial
    OR
    2. The patient has an intolerance or hypersensitivity to two different NSAIDs used in the treatment of AS
    OR
    3. The patient has an FDA labeled contraindication to ALL NSAIDs used in the treatment of AS
    OR
    4. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of AS

OR

i. The patient has a diagnosis of active non-radiographic axial spondyloarthritis (nr-axSpA) AND ONE of the following:
    1. The patient has tried and had an inadequate response to two different NSAIDs used in the treatment of nr-axSpA for at least a 4-week total trial
    OR
    2. The patient has an intolerance or hypersensitivity to two different NSAIDs used in the treatment of nr-axSpA
    OR
    3. The patient has an FDA labeled contraindication to ALL NSAIDs used in the treatment of nr-axSpA
    OR
    4. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of nr-axSpA

OR

j. The patient has a diagnosis of moderately to severely active polyarticular juvenile idiopathic arthritis (PJIA) AND ONE of the following:
    1. The patient has tried and had an inadequate response to ONE conventional agent (i.e., methotrexate, leflunomide) used in the treatment of PJIA for at least 3-months
    OR
    2. The patient has an intolerance or hypersensitivity to ONE of the conventional agents used in the treatment of PJIA
    OR
    3. The patient has an FDA labeled contraindication ALL of the conventional agents used in the treatment of PJIA
    OR
    4. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of PJIA

OR

k. The patient has a diagnosis of active systemic juvenile idiopathic arthritis (SJIA) AND ONE of the following:

1. The patient has tried and had an inadequate response to at least ONE NSAID (e.g., ibuprofen, celecoxib) used in the treatment of SJIA for at least 1-month
   OR
2. The patient has an intolerance or hypersensitivity to NSAIDs used in the treatment of SJIA
   OR
3. The patient has an FDA labeled contraindication to ALL NSAIDs used in the treatment of SJIA
   OR
4. The patient has tried and had an inadequate response to another conventional agent (i.e., methotrexate, leflunomide, systemic corticosteroids) used in the treatment of SJIA for at least 3-months
   OR
5. The patient has an intolerance or hypersensitivity to ONE of the conventional agents used in the treatment of SJIA
   OR
6. The patient has an FDA labeled contraindication to ALL of the conventional agents used in the treatment of SJIA
   OR
7. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of SJIA

OR

l. The patient has a diagnosis of moderate to severe hidradenitis suppurativa (HS) AND ONE of the following:
   1. The patient has tried and had an inadequate response to ONE conventional agent (i.e., oral tetracyclines [doxycycline, minocycline, tetracycline]; oral contraceptives [females only]; metformin [females only]; finasteride [females only]; spironolactone [females only]; intralesional corticosteroids [triamcinolone]; clindamycin in combination with rifampin; combination of rifampin, moxifloxacin, and metronidazole; cyclosporine, oral retinoids) used in the treatment of HS for at least 3-months
      OR
   2. The patient has an intolerance or hypersensitivity to ONE conventional agent used in the treatment of HS
      OR
   3. The patient has an FDA labeled contraindication to ALL conventional agents used in the treatment of HS
      OR
   4. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of HS

OR

m. The patient has a diagnosis of systemic sclerosis associated interstitial lung disease (SSc-ILD) AND BOTH of the following:
   1. The patient's diagnosis has been confirmed on high-resolution computed tomography (HRCT) or chest radiography scans
      AND
   2. ONE of the following:

i. The patient has tried and had an inadequate response to ONE conventional agent (i.e., mycophenolate mofetil, cyclophosphamide, azathioprine) used in the treatment of SSc-ILD
OR
ii. The patient has an intolerance or hypersensitivity to ONE conventional agent used in the treatment of SSc-ILD
OR
iii. The patient has an FDA labeled contraindication to ALL conventional agents used in the treatment of SSc-ILD
OR
iv. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of SSc-ILD

OR

n. The patient has a diagnosis of active enthesitis related arthritis (ERA) and ONE of the following:
    1. The patient has tried and had an inadequate response to two different NSAIDs used in the treatment of ERA for at least a 4-week total trial
    OR
    2. The patient has an intolerance or hypersensitivity to two different NSAIDs used in the treatment of ERA
    OR
    3. The patient has an FDA labeled contraindication to ALL NSAIDs used in the treatment of ERA
    OR
    4. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in compendia for the treatment of ERA

OR

o. The patient has a diagnosis of moderate-to-severe atopic dermatitis (AD) AND ALL of the following:
    1. ONE of the following:
        i. The patient has at least 10% body surface area involvement
        OR
        ii. The patient has involvement of the palms and/or soles of the feet

    AND

    2. ONE of the following:
        i. The patient has tried and had an inadequate response to at least a mid- potency topical steroid used in the treatment of AD for a minimum of 4 weeks **AND** a topical calcineurin inhibitor (e.g., Elidel/pimecrolimus, Protopic/tacrolimus) used in the treatment of AD for a minimum of 6 weeks
        OR
        ii. The patient has an intolerance or hypersensitivity to at least a mid- potency topical steroid AND a topical calcineurin inhibitor (e.g., Elidel/pimecrolimus, Protopic/tacrolimus) used in the treatment of AD

OR

iii. The patient has an FDA labeled contraindication to ALL mid-, high-, and super-potency topical steroids AND topical calcineurin inhibitors used in the treatment of AD

AND

3. ONE of the following**:**
    i. The patient has tried and had an inadequate response to a systemic immunosuppressant, including a biologic, used in the treatment of AD for a minimum of 3 months
    OR
    ii. The patient has an intolerance or hypersensitivity to therapy with systemic immunosuppressants, including a biologic, used in the treatment of AD
    OR
    iii. The patient has an FDA labeled contraindication to ALL systemic immunosuppressants, including biologics, used in the treatment of AD

AND

4. The prescriber has documented the patient's baseline pruritus and other symptom severity (e.g., erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and/or lichenification)

AND

5. BOTH of the following:
    i. The patient is currently treated with topical emollients and practicing good skin care
    AND
    ii. The patient will continue the use of topical emollients and good skin care practices in combination with the requested agent

OR

p. The patient has another FDA labeled indication for the requested agent and route of administration not mentioned previously

OR

q. The patient has another indication that is supported in compendia for the requested agent and route of administration not mentioned previously

AND

iv. ONE of the following (reference Step Table):
    a. The requested indication does NOT require any prerequisite biologic immunomodulator agents
    OR
    b. The requested agent is a Step 1a agent for the requested indication
    OR
    c. If the requested agent is a Step 1b agent for the requested indication, then ONE of the following:
        1. The patient has tried and had an inadequate response to ONE Tumor Necrosis Factor (TNF) inhibitor for the requested indication for at least 3-months (See Step 1a for preferred TNF inhibitors)
        OR
        2. The patient has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or

hypersensitivity to therapy with a TNF inhibitor for the requested indication

OR

3. The patient has an FDA labeled contraindication to ALL TNF inhibitors for the requested indication

OR

4. BOTH of the following:
    i. The prescriber has provided information indicating why ALL TNF inhibitors are not clinically appropriate for the patient

    AND

    ii. The prescriber has provided a complete list of previously tried agents for the requested indication

OR

d. If the requested agent is a Step 2 agent for the requested indication, then ONE of the following:
    1. The patient has tried and had an inadequate response to ONE of the required Step 1 agents for the requested indication for at least 3-months (See Step 2)

    OR

    2. The patient has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to ONE of the required Step 1 agents for the requested indication

    OR

    3. The patient has an FDA labeled contraindication to ALL required Step 1 agents for the requested indication

    OR

    4. BOTH of the following:
        i. The prescriber has provided information indicating why ALL of the required Step 1 agents are not clinically appropriate for the patient

        AND

        ii. The prescriber has provided a complete list of previously tried agents for the requested indication

OR

e. If the requested agent is a Step 3a agent for the requested indication, then ONE of the following (chart notes required):
    1. The patient has tried and had an inadequate response to TWO of the Step 1 agents for the requested indication for at least 3-months (See Step 3a)

    OR

    2. The patient has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration or hypersensitivity to TWO of the Step 1 agents for the requested indication

    OR

    3. The patient has an FDA labeled contraindication to ALL of the Step 1 agents for the requested indication

    OR

    4. BOTH of the following:

i. The prescriber has provided information indicating why ALL of the Step 1 agents are not clinically appropriate for the patient
AND
ii. The prescriber has provided a complete list of previously tried agents for the requested indication

OR

f. If the requested agent is a Step 3b agent for the requested indication, then ONE of the following (chart notes required):
1. The patient has tried and had an inadequate response to TWO agents from Step 1 and/or Step 2 for the requested indication for at least 3-months (See Step 3b)
OR
2. The patient has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to TWO agents from Step 1 and/or Step 2 for the requested indication
OR
3. The patient has an FDA labeled contraindication to ALL of the Step 1 AND Step 2 agents for the requested indication
OR
4. BOTH of the following:
i. The prescriber has provided information indicating why ALL of the Step 1 AND Step 2 agents are not clinically appropriate for the patient
AND
ii. The prescriber has provided a complete list of previously tried agents for the requested indication

OR

g. If the requested agent is a Step 3c agent for the requested indication, then ONE of the following (chart notes required):
1. The patient has tried and had an inadequate response to THREE of the Step 1 agents for the requested indication for at least 3-months (See Step 3c)
OR
2. The patient has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to THREE of the Step 1 agents for the requested indication
OR
3. The patient has an FDA labeled contraindication to ALL of the Step 1 agents for the requested indication
OR
4. BOTH of the following:
i. The prescriber has provided information indicating why ALL of the Step 1 agents are not clinically appropriate for the patient
AND
ii. The prescriber has provided a complete list of previously tried agents for the requested indication

AND

v. If Cosentyx 300 mg every 4 weeks is requested as maintenance dosing, ONE of the following:

a. The patient has a diagnosis of moderate to severe plaque psoriasis with or without coexistent active psoriatic arthritis
OR
b. The patient has a diagnosis of active psoriatic arthritis or active ankylosing spondylitis AND has tried and had an inadequate response to Cosentyx 150 mg every 4 weeks for at least 3-months

AND

2. If Stelara 90 mg is requested, ONE of the following:
   A. The patient has a diagnosis of psoriasis AND weighs >100kg
   OR
   B. The patient has a dual diagnosis of psoriasis AND psoriatic arthritis AND the patient is >100kg
   OR
   C. The patient has a diagnosis of Crohn's disease or ulcerative colitis

AND

3. If Actemra is requested for a diagnosis of systemic sclerosis associated interstitial lung disease, the request is for the Actemra syringe (NOTE: Actemra ACTpen is not approvable for SSc-ILD)

AND

4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., rheumatologist for JIA, PsA, RA; gastroenterologist for CD, UC; dermatologist for PS; pulmonologist, radiologist, pathologist, rheumatologist for SSc-ILD) or has consulted with a specialist in the area of the patient's diagnosis

AND

5. The patient will NOT be using the requested agent in combination with another biologic immunomodulator agent, Zeposia, or Otezla (Please refer to table below "Agents Contraindicated as Concomitant Use")

AND

6. The patient does NOT have any FDA labeled contraindications to the requested agent

AND

7. The patient has been tested for latent tuberculosis (TB) when required by the prescribing information for the requested agent AND if positive the patient has begun therapy for latent TB

AND

8. ONE of the following:
   A. The requested quantity (dose) does NOT exceed the program quantity limit
   OR
   B. If the requested agent is Xeljanz/Xeljanz XR for a diagnosis of ulcerative colitis, then BOTH of the following:
      i. The prescriber has provided information in support of therapy for the dose exceeding the quantity limit [e.g., patient has lost response to the FDA labeled maintenance dose (i.e., 5 mg twice daily or 11 mg once daily) during maintenance treatment; requires restart of induction therapy] (medical records required)
      AND
      ii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit
   OR
   C. If the requested agent is Xeljanz oral solution for a diagnosis of polyarticular course juvenile idiopathic arthritis, then ONE of the following:
      i. BOTH of the following:

1. The requested quantity (dose) does not exceed the maximum FDA labeled dose (i.e., 5 mg twice daily) NOR the maximum compendia supported dose
   AND
2. The prescriber has provided information stating why the patient cannot take Xeljanz 5 mg tablets

OR

ii. The requested quantity (dose) is greater than the maximum FDA labeled dose but does NOT exceed the maximum compendia supported dose for the requested indication

OR

iii. BOTH of the following:
   1. The requested quantity (dose) is greater than the maximum FDA labeled dose AND the maximum compendia supported dose for the requested indication
      AND
   2. The prescriber has provided information in support of therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy required; e.g., clinical trials, phase III studies, guidelines required)

OR

D. If the requested agent is NOT Xeljanz/Xeljanz XR for a diagnosis of ulcerative colitis or polyarticular course juvenile idiopathic arthritis, then ALL of the following:
   i. The requested quantity (dose) is greater than the program quantity limit
      AND
   ii. ONE of the following:
      1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose
         OR
      2. BOTH of the following:
         a. The requested quantity (dose) does NOT exceed the maximum compendia supported dose for the requested indication
            AND
         b. If the requested quantity (dose) is greater than the maximum FDA labeled dose, the patient has tried and had an inadequate response to at least a 3 month trial of the maximum FDA labeled dose (medical records required)

      AND

   iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit

OR

E. If the requested agent is NOT Xeljanz/Xeljanz XR for a diagnosis of ulcerative colitis or polyarticular course juvenile idiopathic arthritis, then ALL of the following:
   i. The requested quantity (dose) is greater than the program quantity limit
      AND
   ii. The requested quantity (dose) is greater than the maximum FDA labeled dose AND the maximum compendia supported dose for the requested indication
      AND
   iii. The patient has tried and had an inadequate response to at least a 3 month trial of the maximum FDA labeled dose (medical records required)
      AND

iv. The prescriber has provided information in support of therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy required; e.g., clinical trials, phase III studies, guidelines required)

Length of Approval: 12 months for all agents EXCEPT Humira (adalimumab) for ulcerative colitis (UC), Siliq for plaque psoriasis (PS), Xeljanz and Xeljanz XR for induction therapy for UC, and the agents with indications that require loading doses for new starts. NOTE: For agents that require a loading dose for a new start, approve the loading dose based on FDA labeling AND the maintenance dose for the remainder of the 12 months. Humira for UC may be approved for 12 weeks, Siliq for PS for 16 weeks, Xeljanz and Xeljanz XR for UC may be approved for 16 weeks.

Compendia Allowed: AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use

**NOTE: Cosentyx for the diagnoses of AS, nr-axSpA, and PSA loading doses are not approvable.

Renewal Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process (*please note Stelara renewal must be for the same strength as the initial approval)
   AND
2. ONE of the following:
   A. The patient had a diagnosis of moderate to severe atopic dermatitis AND BOTH of the following:
      i. The patient has had a reduction or stabilization from baseline (prior to therapy with the requested agent) of ONE of the following:
         A. Affected body surface area
            OR
         B. Flares
            OR
         C. Pruritus, erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and/or lichenification
      AND
      ii. The patient will continue standard maintenance therapies (e.g., topical emollients, good skin care practices) in combination with the requested agent
   OR
   B. The patient has another FDA labeled indication or compendia supported indication AND the patient has had clinical benefit with the requested agent
   AND
3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., rheumatologist for JIA, PsA, RA; gastroenterologist for CD, UC; dermatologist for PS; pulmonologist, radiologist, pathologist, rheumatologist for SSc-ILD) or the prescriber has consulted with a specialist in the area of the patient's diagnosis
   AND
4. The patient will NOT be using the requested agent in combination with another biologic immunomodulator agent, Zeposia, or Otezla (Please refer to table below "Agents Contraindicated as Concomitant Use")
   AND

5. If Cosentyx 300 mg every 4 weeks is requested as maintenance dosing, ONE of the following:
   A. The patient has a diagnosis of moderate to severe plaque psoriasis with or without coexistent active psoriatic arthritis
      OR
   B. The patient has a diagnosis of active psoriatic arthritis or active ankylosing spondylitis AND has tried and had an inadequate response to Cosentyx 150 mg every 4 weeks for at least 3-months

   AND
6. If Actemra is requested for a diagnosis of systemic sclerosis associated interstitial lung disease, the request is for the Actemra syringe (NOTE: Actemra ACTpen is not approvable for SSc-ILD)

   AND
7. The patient does NOT have any FDA labeled contraindications to the requested agent

   AND
8. ONE of the following:
   A. The requested quantity (dose) does NOT exceed the program quantity limit
      OR
   B. If the requested agent is Xeljanz/Xeljanz XR for a diagnosis of ulcerative colitis, then BOTH of the following:
      i. The prescriber has provided information in support of therapy for the dose exceeding the quantity limit [e.g., patient has lost response to the FDA labeled maintenance dose (i.e., 5 mg twice daily or 11 mg once daily) during maintenance treatment; requires restart of induction therapy] (medical records required)
         AND
      ii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit

      OR
   C. If the requested agent is Xeljanz oral solution for a diagnosis of polyarticular course juvenile idiopathic arthritis, then ONE of the following:
      i. BOTH of the following:
         1. The requested quantity (dose) does not exceed the maximum FDA labeled dose (i.e., 5 mg twice daily) NOR the maximum compendia supported dose
            AND
         2. The prescriber has provided information stating why the patient cannot take Xeljanz 5 mg tablets

      OR
      ii. The requested quantity (dose) is greater than the maximum FDA labeled dose but does NOT exceed the maximum compendia supported dose for the requested indication
      OR
      iii. BOTH of the following:
         1. The requested quantity (dose) is greater than the maximum FDA labeled dose AND the maximum compendia supported dose for the requested indication
            AND
         2. The prescriber has provided information in support of therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy required; e.g., clinical trials, phase III studies, guidelines required)

OR

D. If the requested agent is NOT Xeljanz/Xeljanz XR for a diagnosis of ulcerative colitis or polyarticular course juvenile idiopathic arthritis, then ALL of the following:
    i. The requested quantity (dose) is greater than the program quantity limit
    AND
    ii. ONE of the following:
        1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose
        OR
        2. BOTH of the following:
            a. The requested quantity (dose) does NOT exceed the maximum compendia supported dose for the requested indication
            AND
            b. If the requested quantity (dose) is greater than the maximum FDA labeled dose, the patient has tried and had an inadequate response to at least a 3 month trial of the maximum FDA labeled dose (medical records required)

    AND
    iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit

OR

E. If the requested agent is NOT Xeljanz/Xeljanz XR for a diagnosis of ulcerative colitis or polyarticular course juvenile idiopathic arthritis, then ALL of the following:
    i. The requested quantity (dose) is greater than the program quantity limit
    AND
    ii. The requested quantity (dose) is greater than the maximum FDA labeled dose AND the maximum compendia supported dose for the requested indication
    AND
    iii. The patient has tried and had an inadequate response to at least a 3 month trial of the maximum FDA labeled dose (medical records required)
    AND
    iv. The prescriber has provided information in support of therapy with a higher dose or shortened dosing interval for the requested indication (submitted copy required; e.g., clinical trials, phase III studies, guidelines required)

Length of Approval: 12 months

Compendia Allowed: AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use

**NOTE: Cosentyx for the diagnoses of AS, nr-axSpA, and PSA loading doses are not approvable.

