Chronic Inflammatory Disease

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO014

Description

The following biologics and biologic response modifiers are utilized in multiple chronic inflammatory disease states. Most of these agents target cytokines or other inflammatory mediators that are elevated in patients with such disease states. The purpose of this policy is to ensure the appropriate use of these agents.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Medications Included in this Policy

Medication	Indications
abatacept (Orencia®)	• Polyarticular Juvenile Idiopathic Arthritis • Psoriatic Arthritis • Rheumatoid Arthritis
adalimumab (Humira®)	• Ankylosing Spondylitis • Crohn's Disease • Hidradenitis Suppurativa • Polyarticular Juvenile Idiopathic Arthritis • Pediatric Crohn's Disease • Plaque Psoriasis • Psoriatic Arthritis • Ulcerative Colitis • Rheumatoid Arthritis • Uveitis/Panuveitis
anakinra (Kineret®)	• Cryopyrin-Associated Periodic Syndromes (CAPS) (including Chronic Infantile Neurological, Cutaneous and Articular Syndrome (CINCA) or Neonatal-Onset Multisystem Inflammatory Disease (NOMID)) • Rheumatoid Arthritis • Systemic Juvenile Idiopathic Arthritis (off-label)
apremilast (Otezla®)	• Plaque Psoriasis • Psoriatic Arthritis • Behcet Syndrome – ulcer of the mouth
baricitinib (Olumiant®)	• Rheumatoid Arthritis
brodalumab (Siliq®)	• Plaque Psoriasis
certolizumab (Cimzia®)	• Ankylosing Spondylitis

	• Crohn's Disease • Non-radiographic Axial Spondyloarthritis • Plaque Psoriasis • Psoriatic Arthritis • Rheumatoid Arthritis
etanercept (Enbrel®)	• Ankylosing Spondylitis • Plaque Psoriasis • Polyarticular Juvenile Idiopathic Arthritis • Psoriatic Arthritis • Rheumatoid Arthritis
golimumab (Simponi®/Simponi Aria®)	• Ankylosing Spondylitis • Psoriatic Arthritis • Rheumatoid Arthritis • Ulcerative Colitis
guselkumab (Tremfya®)	• Plaque Psoriasis • Psoriatic Arthritis
ixekizumab (Taltz®)	• Ankylosing Spondylitis • Non-radiographic Axial Spondyloarthritis • Plaque Psoriasis • Psoriatic Arthritis
rilonacept (Arcalyst®)	• Cryopyrin-Associated Periodic Syndromes (CAPS) (including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS))
risandizumab (Skyrizi®)	• Plaque Psoriasis
sarilumab (Kevzara®)	• Rheumatoid Arthritis
secukinumab (Cosentyx®)	• Ankylosing Spondylitis • Non-radiographic Axial Spondyloarthritis • Plaque Psoriasis • Psoriatic Arthritis
upadacitinib (Rinvoq™)	• Rheumatoid Arthritis
ustekinumab (Stelara®)	• Crohn's Disease • Adolescent Plaque Psoriasis • Plaque Psoriasis • Psoriatic Arthritis • Ulcerative Colitis
tocilizumab (Actemra®)	• Giant Cell Arteritis • Polyarticular Juvenile Idiopathic Arthritis • Rheumatoid Arthritis • Systemic Juvenile Idiopathic Arthritis
tofacitinib (Xeljanz®)	• Psoriatic Arthritis

	• Rheumatoid Arthritis • Ulcerative Colitis

Applicable to All Disease States and Treatment Options Listed Below

I. Contraindication to one preferred treatment option listed in the policies below does not exempt the requirement to try another required agent prior to biologic approval. For instance, in the rheumatoid arthritis policy to follow, a contraindication to methotrexate but not to other available treatment options (sulfasalazine, hydroxychloroquine, leflunomide, etc.) would not satisfy criteria I(D)(5) In other words, a member would still need to try at least one of these other agents as clinically appropriate.

II. Approved treatments are not to be used in combination with other biologics or other non-biologic specialty medications used to treat autoimmune conditions. Use of TNF blockers such as adalimumab in combination with other biologics, such as anakinra or abatacept, has demonstrated and increased risk of serious infection with insufficient evidence for added benefit. Per product labelings, use of concomitant biologics is not recommended as there is insufficient data to support this. Similarly, non-biologic small molecules such as tofacitinib and baricitinib have not been studied sufficiently with other biologic DMARDs to safely recommend their use as dual therapy. Likewise, sufficient data is not currently available to support the safety and efficacy of apremilast use in combination with other agents listed in this criteria.

Rheumatoid Arthritis

I. **Adalimumab (Humira)** or **etanercept (Enbrel)** may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Member is being managed by or in consultation with a rheumatologist; **AND**
   C. A diagnosis of **rheumatoid arthritis** when the following are met:
      1. Treatment with an oral, non-biologic, non-specialty disease-modifying antirheumatic drug (DMARD) has been ineffective or not tolerated, or all are contraindicated (e.g., guidelines direct to methotrexate, sulfasalazine, hydroxychloroquine, or leflunomide. Other examples include azathioprine and cyclosporine.).

II. **Abatacept (Orencia), anakinra (Kineret), certolizumab (Cimzia), golimumab (Simponi), sarilumab (Kevzara), tocilizumab (Actemra), tofacitinib (Xeljanz/Xeljanz XR), baricitinib (Olumiant), or upadacitinib (Rinvoq)** may be considered medically necessary when the following criteria below are met:
   A. Criteria I(A)-I(C) above are met; **AND**

B. Treatment with adalimumab (Humira) AND etanercept (Enbrel) have been ineffective, contraindicated, or not tolerated.

Renewal Evaluation

I. Member has exhibited improvement or stability of disease symptoms; **AND**
II. The medication prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to rheumatoid arthritis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant, etc.).

Supporting Evidence

I. The agents list above are approved for adult patients in the treatment of rheumatoid arthritis in adult patients based on safety and efficacy data from randomized-controlled trials.
II. The 2015 ACR guidelines recommend the use of DMARD monotherapy (methotrexate preferred) in patients who are DMARD-naïve with early RA. Recommended DMARDs include methotrexate, sulfasalazine, hydroxychloroquine, and leflunomide. The guidelines state azathioprine, cyclosporine, minocycline, and gold were not included due to infrequent use and lack of new data since 2012. For patients with moderate to high disease activity despite adequate trial of DMARD monotherapy, combination DMARD or use of tumor necrosis factor (TNF) inhibitors or non-TNF inhibitor biologics with or without methotrexate is recommended. In patients who have failed both TNF inhibitor and non-TNF inhibitor biologics, or multiple TNF inhibitors, guidelines recommend the use of either another non-TNF biologic or a JAK inhibitor with or without methotrexate. The guidelines do not address the use of baricitinib (Olumiant) given that the medication was approved after the most recent publication. Baricitinib (Olumiant) has demonstrated similar ACR20 responses to tofacitinib (Xeljanz) in clinical trials.
III. The 2016 European League Against Rheumatism (EULAR) guidelines follow similar recommendations to the ACR guidelines, and state that patients who have failed one TNF inhibitor may receive a different TNF inhibitor, as studies have demonstrated primary TNF non-responders have responded to other agents of the same mechanism of action.

References:

1. Singh JA, Saag KG, Bridges SL, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care Res (Hoboken).* 2016;68(1):1-25.
2. Humira [Prescribing Information]. AbbVie Inc.: North Chicago, IL. January 2019.
3. Berglin E, Dahlqvist SR. Comparison of the 1987 ACR and 2010 ACR/EULAR classification criteria for rheumatoid arthritis in clinical practice: a prospective cohort study. *Scand J Rheumatol.* 2013;42(5):362-368.
4. UpToDate, Inc. Diagnosis and differential diagnosis of rheumatoid arthritis. UpToDate [database online]. Waltham, MA. Last updated August 23, 2019. Available at: http://www.uptodate.com/home/index.html.
5. Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis*. 2017;76(6):960-977.

6. Strand V, Schiff M, Tundia N, et al. Patient reported outcomes of upadacitinib: results from biologic inadequate responders (SELECT-BEYOND Phase III trial). Presented at: European League Against Rheumatism (EULAR) – Annual European Congress of Rheumatology: June 13-16, 2018; Amsterdam, The Netherlands. Poster SAT0255.

Polyarticular Juvenile Idiopathic Arthritis (PJIA)

Initial Evaluation

I. **Adalimumab (Humira)** or **etanercept (Enbrel)** may be considered medically necessary when the following criteria below are met:
   A. Member is 2 years of age or older; **AND**
   B. Member is being managed by or in consultation with a rheumatologist; **AND**
   C. A diagnosis of **PJIA** when the following are met:
      1. Treatment with at least one oral, non-biologic, non-specialty disease-modifying antirheumatic drug (DMARD) has been ineffective, contraindicated, or not tolerated. Guidelines direct to use of methotrexate, sulfasalazine, hydroxychloroquine, or leflunomide. Other examples include azathioprine and cyclosporine.

II. **Abatacept (Orencia) or tocilizumab (Actemra)** may be considered medically necessary when the following criteria below are met:
   A. Criteria I(A)-I(C) above are met; **AND**
   B. Treatment with adalimumab (Humira) and etanercept (Enbrel) has been ineffective, contraindicated, or not tolerated.

Renewal Evaluation

I. Member has exhibited improvement or stability of disease symptoms; **AND**
II. Agent prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to rheumatoid arthritis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant)

Supporting Evidence

I. The above agents are approved for pediatric patients greater than two years of age with polyarticular juvenile idiopathic arthritis based on safety and efficacy data from randomized-controlled trials.
II. The 2019 JIA guidelines published by the ACR strongly recommends initial therapy with a DMARD for all patients with JIA and active polyarthritis. For patients both with and without risk factors, initial therapy with a DMARD is recommended over a biologic, though there may be certain situations where a biologic as initial therapy is preferred (i.e. high risk joints such as cervical spine, wrist, or hip involved). ACR notes that while initial treatment with biologics was studied in the TREAT-JIA and ACUTE-JIA studies, results were not deemed conclusive enough to

make recommendations for biologics as initial therapy at this time. For patients with continued moderate to high disease activity, the guidelines recommend adding a TNF inhibitor, abatacept, or tocilizumab.

III. The ACR guidelines make a conditional recommendation for switching to non-TNF inhibitor biologics (tocilizumab and abatacept) in patients receiving a TNF inhibitor with continued moderate or high disease activity. It is noted that a second TNF inhibitor may be appropriate for patients who had a good initial response to the first TNF inhibitor but had secondary failure due to suspected drug antibodies developing, and that this conditional recommendation stems from data in adult rheumatoid arthritis patients.

References

1. Ringold S, Angeles-han ST, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. *Arthritis Care Res (Hoboken).* 2019.
2. UpToDate, Inc. Polyarticular juvenile idiopathic arthritis: treatment. UpToDate [database online]. Waltham, MA. Last updated October 9, 2018. Available at: http://www.uptodate.com/home/index.html.

Systemic Juvenile Idiopathic Arthritis (SJIA)

Initial Evaluation

I. **Anakinra (Kineret)** may be considered medically necessary when the following criteria below are met:
   A. Member is 2 years of age or older; **AND**
   B. Member is being managed by or in consultation with a rheumatologist; **AND**
   C. A diagnosis of **active SJIA** when the following are met:
      1. Treatment with at least one NSAID (e.g. ibuprofen, naproxen, indomethacin, meloxicam, celecoxib, etc.) or glucocorticoid (i.e. prednisone, hydrocortisone, methylprednisolone, etc.) has been ineffective, contraindicated, or not tolerated; **OR**
      2. Patient has severe active disease as indicated by one of the following:
         i. Suspected early macrophage activating syndrome (MAS)
         ii. Disabling polyarthritis
         iii. Serositis

II. **Tocilizumab (Actemra)** may be considered medically necessary when the following criteria below are met:
   A. Criteria I(A)-I(C) above are met; **AND**
   B. Treatment with anakinra (Kineret) has been ineffective, contraindicated, or not tolerated.

III. **Abatacept (Orencia)** may be considered medically necessary when the following criteria below are met:
   A. Criteria I(A)-I(C) above are met; **AND**
   B. Treatment with anakinra (Kineret) and tocilizumab (Actemra) has been ineffective, contraindicated, or not tolerated.

Renewal Evaluation

I. Member has exhibited improvement or stability of disease symptoms; **AND**
II. Agent prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to treat juvenile idiopathic arthritis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant)

Supporting Evidence

I. Anakinra does not have FDA approval for SJIA, but did gain approval recently by the European Medicines Agency for this indication in 2018. A prospective trial examined 42 children with new-onset disease after no response to a seven day trial of NSAIDs. Rapid improvement was seen, with inactive disease noted in 55% and 71% of patients at one and three months, respectively. A similar rate of response was seen in a small, RCT (ANAJIS) to that in the tocilizumab trial described below in terms of ACR30.
II. Tocilizumab is approved for treatment of active SJIA in patients two years and older. In a RCT of 112 children with SJIA for greater than six months who had an inadequate response to NSAIDs and glucocorticoids, tocilizumab patients were more likely to achieve JIA ACR30 response by week 12 compared to placebo (85% vs 24%, $p<0.001$).
III. The SJIA guidelines updated in 2013 by the ACR note that NSAIDs are recommended as an initial treatment approach. Based off expert opinion, however, monotherapy is inappropriate for patients with an MD global assessment score of 5 or greater (0-10 scale), indicating severe disease. Likewise, it is noted that macrophage activation syndrome (MAS) which occurs in approximately 10% of SJIA patients, is a severe, life-threatening condition and delay in IL-1 or IL-6 inhibitor therapy should not occur in this scenario. Anakinra is recommended as an initial treatment option in patients with severely active disease, as well as for patients with continued disease activity after treatment with glucocorticoid or NSAID monotherapy. For those patients who have tried both anakinra and tocilizumab sequentially, abatacept is recommended based off expert opinion. A subset of 37 children with systemic JIA was examined in comparison to placebo in a RCT. After four months of treatment in the initial lead-in period, 24 of 37 patients (65%) treated with abatacept had a ACR30 response, which was similar to response rates in patients included with other JIA subtypes.
IV. TNF inhibitors demonstrate greater efficacy in patients with nonsystemic JIA compared to SJIA. For instance, a study of 45 children who had systemic symptoms at the start of TNF inhibitor

therapy noted lower rates of remission and a high frequency of disease flare (24% and 45%, respectively).

References

1. Ringold S, Weiss PF, Beukelman T, et al. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. *Arthritis Rheum*. 2013;65(10):2499-2512.
2. UpToDate, Inc. Systemic juvenile idiopathic arthritis: treatment. UpToDate [database online]. Waltham, MA. Last updated April 2, 2019. Available at: http://www.uptodate.com/home/index.html.
3. De benedetti F, Brunner HI, Ruperto N, et al. Randomized trial of tocilizumab in systemic juvenile idiopathic arthritis. *N Engl J Med.* 2012;367(25):2385-2395.
4. Ter haar NM, Van dijkhuizen EHP, Swart JF, et al. Treat-to-target using first-line recombinant interleukin-1 receptor antagonist monotherapy in new-onset systemic juvenile idiopathic arthritis: results from a five year follow-up study. *Arthritis Rheumatol*. 2019.
5. Quartier P, Allantaz F, Cimaz R, et al. A multicentre, randomised, double-blind, placebo-controlled trial with the interleukin-1 receptor antagonist anakinra in patients with systemic-onset juvenile idiopathic arthritis (ANAJIS trial). *Ann Rheum Dis.* 2011;70(5):747-754.
6. Russo RA, Katsicas MM. Clinical remission in patients with systemic juvenile idiopathic arthritis treated with anti-tumor necrosis factor agents. *J Rheumatol.* 2009;36(5):1078-1082.
7. Ruperto N, Lovell DJ, Quartier P, et al. Abatacept in children with juvenile idiopathic arthritis: a randomised, double-blind, placebo-controlled withdrawal trial. *Lancet.* 2008;372(9636):383-391.

Psoriatic Arthritis

Initial Evaluation

I. **Adalimumab (Humira)**, **etanercept (Enbrel), or secukinumab (Cosentyx)** may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Member is being managed by or in consultation with a rheumatologist or dermatologist; **AND**
   C. A diagnosis of active **psoriatic arthritis** when the following are met:
      1. Treatment with non-biologic, non-specialty oral small molecules (OSMs) such as methotrexate, leflunomide, sulfasalazine, or cyclosporine has been ineffective, contraindicated, or not tolerated; **OR**
      2. Presence of active, severe disease as indicated by provider assessment and the presence of at least one of the following:
         i. Erosive disease
         ii. Elevated CRP or ESR
         iii. Long-term damage interfering with function (e.g. joint deformities, vision loss)

iv. Major impairment of quality of life due to high disease activity at many sites (including dactylitis, enthesitis,) or functionally-limiting arthritis at a few sites

II. **Abatacept (Orencia), certolizumab (Cimzia), golimumab (Simponi), ixekizumab (Taltz), ustekinumab (Stelara), apremilast (Otezla), tofacitinib (Xeljanz/Xeljanz XR), or guselkumab (Tremfya)** may be considered medically necessary when the following criteria below are met:
   A. Criteria I(A)-I(C) above are met; **AND**
   B. Treatment with adalimumab (Humira), etanercept (Enbrel), AND secukinumab (Cosentyx) has been ineffective, contraindicated, or not tolerated.

**Clinical note: If a patient has a diagnosis of both plaque psoriasis and psoriatic arthritis, approval of the requested medication can be made as long as the patient fulfills the criteria for at least one of the disease states and associated medication criteria.*

Renewal Evaluation

I. Member has exhibited improvement or stability of disease symptoms; **AND**
II. Agent prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to treat psoriatic arthritis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant)

Supporting Evidence

I. The above agents are approved for adult patients in the treatment of psoriatic arthritis based on safety and efficacy data from randomized-controlled trials.
II. The 2018 ACR guidelines make a conditional recommendation for starting a TNF inhibitor over an OSM as a first-line option for patients who are treatment-naïve with active psoriatic arthritis. This recommendation is based on low- to very-low quality of evidence. Many of the studies in which greater benefit was seen in terms of disease severity or radiographic progression compared methotrexate to TNF inhibitors, however, most patients included in these groups were not truly treatment-naïve to OSM medications. Guidelines note that OSM can be used first-line in naïve patients who do not have severe PsA, severe PsO, prefers oral therapy, or has contraindications to TNF inhibitors. In patients who continue to have active disease despite OSM treatment, it is recommended to switch to a TNF inhibitor rather than trying a different OSM.
III. A systematic review of RCTs published in 2015 examined differences in terms of ACR20 response with biologic versus synthetic DMARDs. A statistically significant benefit was not demonstrated with methotrexate, cyclosporine, or sulfasalazine. Leflunomide did demonstrate a statistically significant benefit, though the magnitude of benefit was lower than all of the biologic DMARDs analyzed. There are many limitations to this review, such as a large proportion of trials/data that only included a small number of patients (less than 100). A recent study compared the TNF inhibitor etanercept to methotrexate monotherapy in patients naïve to both biologics and

methotrexate. Patients treated with etanercept were statistically more likely to achieve ACR20 response at week 24 compared to the methotrexate monotherapy group (difference 9.2%, 95% CI 1.0 to 17.3, p = 0.029).

IV. The 2018 guidelines also conditionally recommend for use of a TNF inhibitor biologics over IL-17 inhibitors (ixekizumab, secukinumab) or IL-12/23 inhibitors (ustekinumab). As of August 2020, guidelines have not been updated with regard to place in therapy for guselkumab.

References:

1. Singh JA, Guyatt G, Ogdie A, et al. Special Article: 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. *Arthritis Rheumatol.* 2019;71(1):5-32.
2. Kingsley GH, Scott DL. Assessing the effectiveness of synthetic and biologic disease-modifying antirheumatic drugs in psoriatic arthritis - a systematic review. Psoriasis (Auckl). 2015;5:71-81.
3. Mease PJ, Gladman DD, Samad AS, et al. Design and rationale of the Study of Etanercept and Methotrexate in Combination or as Monotherapy in Subjects with Psoriatic Arthritis (SEAM-PsA). RMD Open. 2018;4(1):e000606.
4. UpToDate, Inc. Treatment of psoriatic arthritis. UpToDate [database online]. Waltham, MA. Last updated November 20, 2018. Available at: http://www.uptodate.com/home/index.html.
5. Deodhar A, Helliwell PS, Boehncke WH, et al. Guselkumab in patients with active psoriatic arthritis who were biologic-naive or had previously received TNFα inhibitor treatment (DISCOVER-1): a double-blind, randomised, placebo-controlled phase 3 trial [published correction appears in Lancet. 2020 Apr 4;395(10230):1114]. Lancet. 2020;395(10230):1115-1125. doi:10.1016/S0140-6736(20)30265-8
6. Mease PJ, Rahman P, Gottlieb AB, et al. Guselkumab in biologic-naive patients with active psoriatic arthritis (DISCOVER-2): a double-blind, randomised, placebo-controlled phase 3 trial [published correction appears in Lancet. 2020 Apr 4;395(10230):1114]. Lancet. 2020;395(10230):1126-1136. doi:10.1016/S0140-6736(20)30263-4

Ankylosing Spondylitis

Initial Evaluation

I. **Adalimumab (Humira)**, **etanercept (Enbrel)**, or **secukinumab (Cosentyx)** may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Member is being managed by or in consultation with a rheumatologist; **AND**
   C. A diagnosis of **ankylosing spondylitis** when the following are met:
      1. High disease activity as indicated by BASDAI score of at least 4 or ASDAS score of at least 2.1; **AND**
      2. Treatment with at least two different NSAIDs (e.g. indomethacin, meloxicam, celecoxib, naproxen, nabumetone, etc.) over four weeks has been ineffective, contraindicated, or not tolerated; **AND**
      3. Disease manifested as axial disease; **OR**
      4. Disease manifested as peripheral arthritis.

II. **Certolizumab (Cimzia), ixekizumab (Taltz), and golimumab (Simponi)** may be considered medically necessary when the following criteria below are met:
   A. Criteria I(A)-I(C) above are met; **AND**

B. Treatment with adalimumab (Humira), etanercept (Enbrel), and secukinumab (Cosentyx) has been ineffective, contraindicated, or not tolerated.

Renewal Evaluation

I. Member has exhibited improvement or stability of disease symptoms; **AND**
II. Agent prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to treat psoriatic arthritis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant)

Supporting Evidence

I. The above agents are approved for adult patients in the treatment of ankylosing spondylitis based on safety and efficacy data from randomized-controlled trials.
II. The 2015 ACR and Spondylitis Association of America (SAA) guidelines on the treatment of ankylosing spondylitis strongly recommend the use of NSAIDs as first-line treatment (with 70-80% responding). For those patient with inadequate response despite continuous NSAID treatment, the ACR strongly recommends use of TNF inhibitors. For those patients with continued active disease, the ACR conditionally recommends trial of a different TNF inhibitor over treatment with a non-TNF inhibitor biologic. Observational studies have demonstrated clinical improvement in patients who have switched TNF inhibitors compared to switching to a DMARD or non-TNF biologic. The 2016 ASAS/EULAR guideline update mirrors that of the ACR/SAA. NSAIDs are also noted as first-line treatment due to robust response of greater than 70% of patients achieving ASAS20, and greater than 50% of patients achieving ASAS40 response. Recommendations against the use of non-biologic DMARDs are made for patients with purely axial disease, however, sulfasalazine may be considered in patients with peripheral disease. In order to qualify for treatment with biologics, ASAS/EULAR recommends patients try and fail at least 2 NSAIDs over 4 weeks, have a trial of glucocorticoid injection or sulfasalazine if peripheral symptoms, and have a high disease activity as defined by a BASDAI of at least 4 or an ASDAS of at least 2.1. The update to the guidelines in 2016 notes that if a patient fails TNF inhibitor therapy, switching to another TNF inhibitor of IL-17 inhibitor can be considered.
III. The ACR conditionally recommends against the use of DMARDs in patients with ankylosing spondylitis that remains active despite NSAID treatment. This is based off controlled trials demonstrating minimal to no benefit with agents such as sulfasalazine, methotrexate, and leflunomide. Some benefit has been seen in patients with peripheral arthritis, and thus these agents may be considered for patients with ankylosing spondylitis with predominantly peripheral arthritis symptoms.

References:

1. Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. *Arthritis Rheumatol*. 2016;68(2):282-298.
2. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis*. 2016;75(3):499-510.
3. Van der heijde D, Ramiro S, Landewé R, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis.* 2017;76(6):978-991.
4. Van der heijde D, Sieper J, Maksymowych WP, et al. 2010 Update of the international ASAS recommendations for the use of anti-TNF agents in patients with axial spondyloarthritis. *Ann Rheum Dis*. 2011;70(6):905-908.
5. UpToDate, Inc. Treatment of axial spondyloarthritis (ankylosing spondylitis and nonradiographic axial spondloarthritis) in adults. UpToDate [database online]. Waltham, MA. Last updated April 4, 2019. Available at: http://www.uptodate.com/home/index.html.
6. UpToDate, Inc. Treatment of peripheral spondyloarthritis. UpToDate [database online]. Waltham, MA. Last updated February 28, 2019. Available at: http://www.uptodate.com/home/index.html.

Non-radiographic Axial Spondyloarthritis

Initial Evaluation

I. **Adalimumab (Humira), Etanercept (Enbrel), or secukinumab (Cosentyx)** may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Member is being managed by or in consultation with a rheumatologist; **AND**
   C. A diagnosis of **non-radiographic axial spondyloarthritis** when the following are met:
      1. High disease activity as indicated by BASDAI score of at least 4 or ASDAS score of at least 2.1; **AND**
      2. Treatment with at least two different NSAIDs (e.g. indomethacin, meloxicam, celecoxib, naproxen, nabumetone, etc.) over four weeks has been ineffective, contraindicated, or not tolerated; **AND**
      3. Disease manifested as axial disease; **OR**
      4. Disease manifested as peripheral arthritis.

II. **Certolizumab (Cimzia) or ixekizumab (Taltz)** may be considered medically necessary when the following criteria below are met:
   A. Criteria I(A)-I(C) above are met; **AND**
   B. Treatment with adalimumab (Humira), etanercept (Enbrel), and secukinumab (Cosentyx) has been ineffective, contraindicated, or not tolerated.

Renewal Evaluation

I. Member has exhibited improvement or stability of disease symptoms; **AND**
II. Agent prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to treat psoriatic arthritis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant)

Supporting Evidence

I. Currently, certolizumab pegol, ixekizumab, and secukinumab are the only FDA approved agent for adults with non-radiographic axial spondyloarthritis. Other TNF inhibitors are approved in Europe for this indication, have demonstrated efficacy in RCTs, and are utilized frequently in clinical practice. For instance, a study of 192 patients taking adalimumab demonstrated significant improvement compared to placebo in ASAS40 response by week 12 in patients with non-radiographic disease (36% vs 15%, $p < 0.001$). Likewise, etanercept and golimumab have also been approved by the European Medicines Agency, and the 2016 ASAS/EULAR guidelines note that efficacy in regards to musculoskeletal signs and symptoms appears comparable based off indirect comparison.

II. A phase 3 double-blind, randomized, placebo-controlled trial (C-AXSPAND) examined the use of certolizumab pegol in patients with non-radiographic axial spondyloarthritis who had an inadequate response to at least two prior NSAIDs. In terms of the primary endpoint of patients achieving a response in the Ankylosing Spondylitis Disease Activity Score-Major Improvement (ASDAS-MI) at week 52, a significantly more patients in the certolizumab pegol group achieved this clinical response compared to placebo (47% vs 7%, OR 15.2, 95% CI 7.3 to 31.6). Improvement was also seen in secondary outcomes such as quality of life questionnaires.

III. A phase 3, double-blind, randomized, parallel-group, placebo-controlled trial (COAST-X) assessed the use of ixekizumab in patients with non-radiographic axial spondyloarthritis who had an inadequate response to at least two prior NSAIDs. Primary endpoint of Assessment of Spondyloarthritis International Society 40 (ASAS40) response at weeks 16 and 52 on ixekizumab 80 mg every four weeks compared to placebo was achieved (week 16: 35% vs 19%, OR 2.36, 95% CI 1.23-4.51, p=0.0094, and week 52: 30% vs 13%, OR 2.82, 95% CI 1.38-5.77, p=0.0045). Improvement was also seen in secondary outcomes such as Ankylosing Spondylitis Disease Activity Score (ASDAS) and quality of life.

IV. A phase 3, double-blind, randomized, placebo-controlled trial (PREVENT) assessed the use of secukinumab in patients with non-radiographic axial spondyloarthritis who had active disease (BASDAI greater or equal to four, visual analogue scale (VAS) for total back pain greater or equal to 40) despite NSAID therapy. Primary endpoints of Assessment of Spondyloarthritis International Society 40 (ASAS40) response at week 16 in TNFi-naïve patients on secukinumab 150 mg with loading dose compared to placebo and ASAS40 response at week 52 in TNFi-naïve patients on secukinumab 150 mg without loading dose compared to placebo were achieved (week 16: 41.5% vs 29.2%, p=0.0197, and week 52: 39.8% vs 19.9%, p<0.0021). Improvement was seen in secondary outcomes at week 16 for Ankylosing Spondylitis Disease Activity Score (ASDAS) and quality of life.

V. Per 2019 ACR non-radiographic axial spondyloarthritis treatment guidelines, the panel strongly recommends treatment with TNF inhibitors over no treatment with TNF inhibitors. Moreover, the panel conditionally recommends treatment with TNF inhibitors over treatment with

secukinumab or ixekizumab, and conditionally recommends treatment with secukinumab or ixekizumab over tofacitinib. In patients with primary nonresponse to the first TNF inhibitor, the panel conditionally recommends switching to secukinumab or ixekizumab over switching to a different TNF inhibitor. A systematic review by Corbett et al published in 2016 demonstrated significant improvement in disease state measures such as the ASAS20 and BASDAI50 in patients with non-radiographic axial spondyloarthritis taking TNF inhibitors such as adalimumab, certolizumab pegol, etanercept, and infliximab. The 2016 guideline update by ASAS/EULAR notes that there is still some debate as to whether the two diseases (radiographic and non-radiographic) should be considered as two different entities, given that some patients with non-radiographic disease may develop radiographic changes over time (and some may not).

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Plaque Psoriasis

Initial Evaluation

I. **Adalimumab (Humira), etanercept (Enbrel), secukinumab (Cosentyx), or risankizumab (Skyrizi)** may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older if prescribed adalimumab (Humira), sekukinumab (Cosentyx), or risankizumab (Skyrizi); **OR**
      1. Member is 4 years of age or older if prescribed etanercept (Enbrel); **AND**
   B. Member is being managed by or in consultation with a dermatologist; **AND**
   C. A diagnosis of **moderate to severe plaque psoriasis** when the following are met:
      1. Chronic disease (greater than 6 months), and at least 10% of body surface area is involved or involves areas of the face, ears, hands, feet or genitalia; **AND**

2. Treatment with the following has been ineffective or not tolerated, or all are contraindicated:
    i. Phototherapy (UVB or PUVA); **OR**
    ii. At least one non-biologic, non-specialty DMARD (e.g. methotrexate, cyclosporine, acitretin, azathioprine, etc.)

II. **Apremilast (Otezla), brodalumab (Siliq), certolizumab (Cimzia), guselkumab (Tremfya), ixekizumab (Taltz), and ustekinumab (Stelara)** may be considered medically necessary when the following criteria below are met:
    A. Criteria I(A)-I(C) above are met; **AND**
    B. Treatment with adalimumab (Humira), etanercept (Enbrel), secukinumab (Cosentyx) AND risankizumab (Skyrizi) have all been ineffective, contraindicated, or not tolerated; **AND**
    C. The member is 18 years of age or older, if prescribed apremilast (Otezla), brodalumab (Siliq), certolizumab (Cimzia), or guselkumab (Tremfya); **OR**
    D. The request is for ustekinumab (Stelara); **AND**
        1. The member is 6 years of age or older; **OR**
    E. The request is for ixekizumab (Taltz); **AND**
        1. Member is 6 years of age or older; **AND**
        2. Member has a body weight > 50 kg (110 lb)

Renewal Evaluation

I. Member has exhibited improvement or stability of disease symptoms; **AND**
II. The medication prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to treat psoriatic arthritis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant, Rinvoq).

Supporting Evidence

I. The above agents are approved in the treatment of moderate to severe plaque psoriasis based on safety and efficacy data from randomized-controlled trials.
II. The American Academy of Dermatology (AAD) and National Psoriasis Foundation (NPF) published a joint guideline in 2019 on the use of biologic agents in plaque psoriasis. The guidelines state that a majority of patients with mild-to-moderate disease (<10% BSA) are capable of controlling the disease solely with topical mediations or phototherapy. The guideline provides a strong recommendation for use of TNF inhibitor monotherapy in patients with moderate to severe plaque psoriasis.
III. Non-TNF inhibitor biologics are also recommended as monotherapy in patients with moderate to severe plaque psoriasis according to the AAD/NPF guidelines. While specific recommendations for choice of treatment are not made, head-to-head studies have suggested IL-17 inhibitors may be more effective for some patients. For instance, the CLEAR study which compared secukinumab (Cosentyx) to ustekinumab (Stelara) found that at week 16

secukinumab (Cosentyx) patients were more likely to have achieved a Psoriasis Area and Severity Index (PASI) 90 response. Similar results have been demonstrated when compared to TNF inhibitors. For instance, in the FIXTURE study, secukinumab (Cosentyx) patients had a statistically significant superior 77.1% PASI 75 response rate compared to 44% with etanercept (Enbrel).

IV. At this time, the AAD/NPF states that there is insufficient data to make specific recommendations regarding switching from one biologic treatment to another. A number of studies have demonstrated response after switching from one TNF inhibitor to another. For instance, in the BELIEVE study, 61.7% of the 448 patients who had received prior TNF inhibitor treatment for plaque psoriasis demonstrated a PASI 75 response by week 16 after switching to adalimumab.

V. Risankizumab (Skyrizi) was evaluated in four Phase 3, randomized-controlled trials, the SELECT-clinical trials program. Various patient populations were evaluated, from treatment naïve to several (3+) biologic failures. Risankizumab (Skyrizi) showed superiority to methotrexate, other oral DMARDS, adalimumab (Humira), and ustekinumab (Stelara) in PASI 90, PASI 100, sPGA scores, and patient reported outcomes in all trials. The evidence was considered high quality due to the multiple RCTs, placebo and active controlled trials, statistically and clinically meaningful outcomes, and large magnitudes of effect.

VI. Ustekinumab (Stelara) was evaluated in pediatric populations 6 years or older, in a phase III, open-label, single arm trial as part of the CADMUS clinical trial program. The CADMUS JR clinical trial (N=44) evaluated efficacy and safety of weight-based dosing of ustekinumab (Stelara) in patients 6 to 12 years old with moderate to severe plaque psoriasis. Primary endpoint was proportion of patients achieving sPGA 0/1 at week 12. Significant secondary outcomes included improvement in PASI responses (PASI 75, PASI90), pharmacokinetics (PK), and biomarker analysis. At week 12, 77% subjects achieved a sPGA 0/1, with 84% and 64% reporting PASI75 and PASI90, respectively. Although this trial consisted of a small population size and an open-label design, PK parameters and biomarker analysis (IL-17 and IL-22 serum levels) helped correlate the observed efficacy with the physiological effects of Stelara. Overall quality of evidence is considered low to moderate.

VII. In a phase III double-blind RCT (IXORA-PEDS), ixekizumab (Taltz) was compared with placebo for efficacy and safety in pediatric populations (N=171, age 6 to < 18 years). Primary endpoints were PASI response (PASI75) and sPGA 0/1 at week 12. Ixekizumab (Taltz) showed superiority to placebo at week 12 with PASI75 response in 89% and 25% of the patients in treatment arm and the placebo arm, respectively. At week 12, 81% (N= 93) patients on Taltz achieved a sPGA of 0 or 1 as compared to 9.8% to those in placebo arm. Due to a small sample size (N=2, 1.16%), clinical applicability of ixekizumab (Taltz) in patients with a body weight of < 25 kg is uncertain and the quality of evidence in this patient subset is considered low. Additionally, patients weighing < 50 kg require administration of ixekizumab (Taltz) by a healthcare professional. Therefore, coverage of Taltz for patients < 50 kg body weight should be considered under the members medical benefits.

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Crohn's Disease

Initial Evaluation

I. **Adalimumab (Humira)** may be considered medically necessary when the following criteria below are met:
   A. Member is 6 years of age or older; **AND**
   B. Member is being managed by or in consultation with a gastroenterologist; **AND**
   C. A diagnosis of **moderate to severe Crohn's disease** when the following are met:
      1. Presence of at least one of the following:
         i. Crohn's Disease Activity Index (CDAI) score ≥ 220
         ii. Prominent symptoms (fever, weight loss, abdominal pain/tenderness, intermittent nausea/vomiting, weight loss, and/or significant anemia)
         iii. Mucosal disease evident on endoscopy; **AND**
      2. Treatment with oral corticosteroids (i.e. prednisone, hydrocortisone, methylprednisolone, etc.) used short-term to induce remission or alleviate signs/symptoms of disease flare has been ineffective, contraindicated, or not tolerated; **AND**

3. Treatment with at least one immunomodulatory agents (e.g. methotrexate, azathioprine, 6-mercaptopurine) over an eight week period to maintain remission has been ineffective, contraindicated, or not tolerated; **OR**

D. A diagnosis of **severe/fulminant Crohn's disease** when the following are met:
   1. Presence of at least one of the following:
      i. CDAI score > 450
      ii. Prominent symptoms (persistent vomiting, involuntary guarding/rebound tenderness, and/or cachexia)
      iii. Evidence of abscess or intestinal obstruction
      iv. Severe mucosal disease evident on endoscopy; **AND**
   2. Treatment with IV corticosteroids (i.e. methylprednisolone) has been ineffective, contraindicated, or not tolerated.

E. A diagnosis of **Crohn's disease with surgical resection completed or planned** when the following are met:
   1. Presence of at least one of the following:
      i. Current smoker
      ii. Penetrating disease (i.e. fistulas, abscess, and/or intestinal perforation) with no history of previous surgical resection
      iii. Two or more previous surgeries or prior surgical resection in the past ten years.

II. **Certolizumab pegol (Cimzia) and ustekinumab (Stelara)** may be considered medically necessary when the following criteria below are met:
   A. Criteria I(B)-I(E) above are met*; **AND**
   B. Member is 18 years of age or older; **AND**
   C. Treatment with adalimumab (Humira) has been ineffective, contraindicated, or not tolerated.

Renewal Evaluation

I. Member has exhibited improvement or stability of disease symptoms; **AND**
II. Agent prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to treat psoriatic arthritis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant)

Supporting Evidence

I. The above agents are approved in the treatment of moderate to severe Crohn's disease based on safety and efficacy data from randomized-controlled trials. Per package labeling, adalimumab (Humira) is FDA-approved for use in pediatrics. Certolizumab pegol (Cimzia) and ustekinumab (Stelara) are approved in adults only.

II. The American College of Gastroenterology (ACG) guidelines on the management of Crohn's disease in adults was published in 2018. In patients with moderately to severely active disease as ACG describes above, a strong recommendation if made for the use of TNF inhibitors in patients who are resistant to treatment with corticosteroids and when refractory to thiopurines or methotrexate when used for maintaining remission.

III. The ACG states that ustekinumab (Stelara) should be given for moderate to severe disease in patients who failed previous treatment with corticosteroids, thiopurines, methotrexate, or TNF inhibitors. To date, no head-to-head trials are available comparing ustekinumab to TNF inhibitors or anti-integrin therapies (natalizumab and vedolizumab). A study is currently recruiting to compare the efficacy of ustekinumab to adalimumab in patients with Crohn's disease.

IV. ACG guidelines note that TNF inhibitors such as infliximab, adalimumab, and certolizumab pegol can be considered to treat severely active/fulminant Crohn's disease. This recommendation stems from clinical expertise, as patients with CDAI scores greater than 450 indicating severe disease were excluded from clinical trials.

V. Guidelines also describe the recommendations for patients in the postoperative setting to prevent recurrence of disease flare. It is noted that in high-risk patients as indicated by the risk factors described above, TNF inhibitors should be started within 4 weeks of surgery to prevent postoperative recurrence. Meta-analyses of the use of thiopurines in this setting have provided varying results, and therefore these agents may be more appropriate in low-risk surgical patients. Meta-analyses have demonstrated consistent results with the TNF inhibitors in preventing recurrence in postoperative patients.

References:

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Ulcerative Colitis

Initial Evaluation

I. **Adalimumab (Humira)** may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Member is being managed by or in consultation with a gastroenterologist; **AND**
   C. A diagnosis of **moderate to severe ulcerative colitis** when the following are met:

1. Previous treatment with at least one systemic corticosteroid (e.g. prednisone, hydrocortisone, methylprednisolone, etc.) has been ineffective to induce remission, contraindicated, or not tolerated; **AND**
2. Previous treatment with at least one thiopurine (azathioprine or 6-mercaptopurine) over an eight week period to maintain remission has been ineffective, contraindicated, or not tolerated

II. **Golimumab (Simponi), ustekinumab (Stelara), and tofacitinib (Xeljanz/Xeljanz XR)** may be considered medically necessary when the following criteria below are met:
   A. Criteria I(A)-I(C) above are met; **AND**
   B. Treatment with adalimumab (Humira) has been ineffective, contraindicated, or not tolerated.

Renewal Evaluation

I. Member has exhibited improvement or stability of disease symptoms; **AND**
II. Agent prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to treat psoriatic arthritis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant)

Supporting Evidence

I. The above agents are approved in the treatment of moderate to severe ulcerative colitis based on safety and efficacy data from randomized-controlled trials.
II. The ACG published guidelines on the management of ulcerative colitis in adults recently in 2019. In patients with moderately to severely active disease to any extent, a strong recommendation is made for the use of oral systemic corticosteroids to induce disease remission. TNF inhibitors, vedolizumab, and tofacitinib also carry similar strong recommendations for induction of remission. For patients achieving remission, a conditional recommendation is made to use thiopurine therapy (and to avoid methotrexate therapy) to maintain remission. The guidelines note that a systematic review of 1,632 patients with UC that encompassed 30 studies demonstrated that azathioprine and mercaptopurine had a 76% mean efficacy in maintaining remission. For those patients initially using a biologic of tofacitinib to induce remission, guidelines support continuing with the same agent to maintain remission.
III. In two phase 3 double-blind RCTs (ULTRA-1 and ULTRA-2) comparing adalimumab to placebo in patients with moderately to severely active ulcerative colitis, patients were included if they were on a stable dose of systemic corticosteroids prior to baseline and/or underwent at least a 90 day course of thiopurine therapy prior to baseline. Based off this inclusion criteria, adalimumab is FDA approved in patients who had an inadequate response to corticosteroids and/or thiopurines.

References:

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2. Reinisch W, Sandborn WJ, Panaccione R, et al. 52-week efficacy of adalimumab in patients with moderately to severely active ulcerative colitis who failed corticosteroids and/or immunosuppressants*. Inflamm Bowel Dis.* 2013;19(8):1700-1709.
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Behcet's Disease (i.e., Behcet Syndrome)

Initial Evaluation

I. **Adalimumab (Humira) OR etanercept (Enbrel)** may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Member is being managed by or in consultation with a specialist that is treatment this condition (e.g., rheumatologist, dermatologist, ophthalmologist, etc.); **AND (one of the following)**
      1. A diagnosis of recurrent **Behcet's Disease manifesting as oral ulcers of the mouth**; **AND**
         i. All of the following have been ineffective, not tolerated, or are contraindicated:
            a. Topical corticosteroids (e.g., triamcinolon) OR sucralfate mouthwash; **AND**
            b. Oral corticosteroids; **OR**
      2. A diagnosis of **Behcet's disease manifesting as uveitis**; **AND**
         i. All of the following have been ineffective, not tolerated, or are contraindicated;
            a. Oral corticosteroids; **AND**
            b. At least one non-biologic, non-specialty DMARD (e.g., methotrexate, cyclosporine, acitretin, azathioprine, etc.).

II. **Apremilast (Otezla)** may be considered medically necessary when the following criteria below are met:
   A. Criteria I(A)-I(B1) above are met (i.e., apremilast [Otezla] would only be appropriate for Behcet's disease manifesting as oral ulcers of the mouth); **AND**
   B. Treatment with adalimumab (Humira) **OR** etanercept (Enbrel) been ineffective, contraindicated, or not tolerated.

Renewal Evaluation

I. Member has exhibited improvement of disease symptoms (reduction in inflammation, and/or lesions, reduction in amount of oral glucocorticoids needed, reduction in number of flares, etc.); **AND**

II. The medication prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to treat psoriatic arthritis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant, Rinvoq).

Supporting Evidence

I. Adalimumab (Humira) and Etanercept (Enbrel) are not FDA-approved for the treatment of any manifestation of Behcet's Disease; however, several studies are available to support the use of these agents for various manifestations of the disease. Notably, mouth ulcers and ophthalmic complications. Examples are provided below.
   - Trial of etanercept in Behcet's Disease, double blind, placebo controlled trial: 40 patients with mucocutaneous disease were enrolled in a trial evaluating etancercept compared to placebo. Results indicated efficacy of etanercept on oral ulcers, nodular lesions, papulopustular lesions, and had an increased probability of being ulcer and nodular lesion free compared to the placebo group. Although a small trial, the rarity of Behcet's Disease shall be taken into account.
   - A multicenter study of refractory Behcet's Disease treated with and-TNF alpha treatments was conducted: The trial included infliximab and adalimumab. These therapies resulted in an overall 90.4% response rate for all clinical manifestations, and specifically an 88% response rate for mucocutaneous manifestations and 96.3% for severe and/or refractory ocular disease. The incidence of flares was reduced during anti-TNF alpha treatment.
   - An analysis of published data in 369 patients using anti-TNF alpha agents for Behcet's Disease: This included peer-reviewed articles on Medline/PubMed, and evaluated patients that were uncontrolled with or intolerant to other immunosuppressives. A rate of 90% clinical response was seen for the mucocutaneous manifestations of Behcet's disease, and a rate of 89% for ocular disease.

II. Corticosteroids and oral DMARDS (typically azathioprine) have been mainstays of Behcet's Disease, with oral DMARDS having a particular role in ophthalmic manifestations.

III. For oral manifestations first line treatment is triamcinolone acetonide cream 0.1% in orabase, applied three to four times daily. High potency steroids may also be employed. Topical sucralfate may also be used with or as an alternative to topical corticosteroids. A strength of 1 gram/5 mL four times daily as a mouthwash is recommended to reduce pain, frequency, and healing time.

IV. Behcet's Disease may manifest in many forms; however, it is commonly managed by rheumatology specialists; however, there may be instances when other inflammatory specialists may be managing and prescribing.

V. Apremilast (Otezla) was evaluated for Behcet's Disease in the following trial: Efficacy of apremilast for oral ulcers associated with active Behcet's Syndrome in a Phase III study. This indication was FDA-approved for treatment of oral ulcers of the mouth associated with Behcet's Disease in July 2019. A total of 207 patients were randomized to apremilast or placebo, and favorable treatment effect was noted. Although apremilast is an FDA-approved medication for Behcet's Disease, anti-TNF alpha therapies have equal or greater safety and efficacy data to support their use in this condition. Guidelines and key opinion leaders have consensus in regards to use of anti-TNF alpha therapies prior to use of apremilast; however, due to limited evidence of using one anti-TNF alpha agent after failure of another, trial of more than one agent is not required.

VI. Standard dosing for adalimumab (Humira) is 40 mg every other week, and standard dosing for Etanercept (Enbrel) is 50 mg per week, either 25 mg twice weekly or 50 mg once weekly.

References:

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Hidradenitis Suppurativa

Initial Evaluation

I. **Adalimumab (Humira)** may be considered medically necessary when the following criteria below are met:
   A. Member is 12 years of age or older; **AND**
   B. Member is being managed by or in consultation with a dermatologist; **AND**
   C. A diagnosis of **hidradenitis suppurativa** when the following are met:
      1. Presence of inflammatory nodules and/or abscesses; **AND**
      2. Hurley Stage III (severe) disease; **OR**
      3. Hurley Stage II (moderate) disease with:
         i. Treatment with at least one oral antibiotic (i.e. doxycycline, minocycline, tetracycline, clindamycin/rifampin, etc.) has been ineffective, contraindicated, or not tolerated

Renewal Evaluation

I. Member has exhibited improvement or stability of disease symptoms; **AND**
II. Agent prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to treat psoriatic arthritis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant)

Supporting Evidence

I. Adalimumab (Humira) is FDA-approved for HS in patients in 12 years or older with moderate to severe disease based off results of the PIONEER I and II RCTs.
II. In the PIONEER studies, patients were only included if they had a diagnosis of Hurley Stage II or Hurley Stage III disease, had at least three inflammatory nodules/abscesses present at baseline, and had previously had an inadequate response to at least a 3-month trial of oral antibiotics. This mirrors the recent evidence-based guidelines published by the British Association of Dermatologists which recommends adalimumab use be reserved for patients with moderate to severe disease that is unresponsive to more conventional systemic therapies (i.e. antibiotics).
III. While oral antibiotics are frequently employed in moderate to severe disease as noted above, the data for these agents primarily stems from studies in patients with Hurley Stage I and II disease. While the combination of clindamycin/rifampin has demonstrated improvement in terms of partial or total remission, only one small study with 10 patients has examined the use in Hurley Stage III patients. The European Dermatology Forum evidence review notes this, and suggests that adalimumab be considered for first-line treatment in patients with more severe disease. Nearly 50% of patients in the PIONEER I and II studies of adalimumab had Hurley Stage III disease, and the randomized, controlled nature of the study provides greater assurance of efficacy for this more severe population than prior studies of oral antibiotics.

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Uveitis and Panuveitis

Initial Evaluation

I. **Adalimumab (Humira)** may be considered medically necessary when the following criteria below are met:
   A. Member is two years of age or older; **AND**
   B. Member is being managed by or in consultation with an ophthalmologist or rheumatologist; **AND**
   C. A diagnosis of **non-infectious intermediate, posterior, or panuveitis** when the following are met:
      1. Previous treatment with at least one periocular injection, implant, topical, or systemic corticosteroid (i.e. triamcinolone, dexamethasone, prednisone, fluocinolone, difluprednate, etc.) has been ineffective, contraindicated, or not tolerated; **AND**
      2. Previous treatment with at least one noncorticosteroid systemic immunomodulatory therapy (i.e. mycophenolate mofetil, tacrolimus, cyclosporine, azathioprine, or methotrexate) has been ineffective, contraindicated, or not tolerated.

Renewal Evaluation

I. Member has exhibited improvement or stability of disease symptoms; **AND**
II. Agent prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to treat psoriatic arthritis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant)

Supporting Evidence

I. Adalimumab (Humira) is FDA-approved for patients at least two years of age with non-infectious intermediate, posterior, or panuveitis based off data from the VISUAL I and II phase 3 RCTs.
II. The Fundamentals of Care for Uveitis (FOCUS) guideline recommends that the noncorticosteroid systemic immunomodulatory therapy (NCIST) agents listed above may be indicated for patients who have a failure or lack of tolerance to regional or systemic corticosteroids. Prior to initiation of alternative medications such as biologic agents, guidelines recommend dose escalation to the maximum tolerated/effective dose of NCIST. It is noted that use of biologic agents is supported for adalimumab, infliximab, and interferon alpha-2a.
III. A meta-analysis published recently in 2018 supports this statement of biologic utility in uveitis. The analysis included 3 RCTs and 20 non-RCTs that examined adalimumab use in patients with non-infectious uveitis, with reduced time to treatment failure and improvements in visual acuity demonstrated.

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Giant Cell Arteritis

Initial Evaluation

I. **Tocilizumab (Actemra)** may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Member is being managed by or in consultation with a rheumatologist; **AND**
   C. A diagnosis of **giant cell arteritis** when the following are met:
      1. Presence of at least three of the following:
         i. Age at disease onset of at least 50 years
         ii. New onset headache at time of diagnosis
         iii. Temporary artery abnormality (tenderness to palpation or decreased pulsation)
         iv. Elevated ESR
         v. Abnormal artery biopsy; **AND**
      2. Previous treatment with at least one glucocorticoids (i.e. prednisone, hydrocortisone, methylprednisolone, etc.) and attempted dose reduction/taper has been ineffective, contraindicated, or not tolerated.

Renewal Evaluation

I. Member has exhibited improvement or stability of disease symptoms; **AND**
II. Agent prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to treat psoriatic arthritis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant)

Supporting Evidence

I. Tocilizumab (Actemra) is FDA-approved for adult patients with giant cell arteritis based off results of a phase 3 RCT. In this trial, 251 patients were randomized to subcutaneous tocilizumab plus a prednisone taper or placebo plus a prednisone taper. The primary outcome of

glucocorticoid-free remission statistically significant, with 53% and 56% (weekly and every other week dosing, respectively) of tocilizumab patients having sustained remission at week 52, compared to 14% and 18% (26-week versus 52-week taper, respectively) of prednisone patients ($p < 0.001$).

II. The 1990 ACR criteria for giant cell arteritis has been demonstrated to have a sensitivity of 93.5% and a specificity of 91.2%. Newer criteria were proposed in 2012 by a collaborative effort of EULAR/ACR that aimed to reduce the need for arterial biopsy. The newer criteria thus has a lower sensitivity (68%) and specificity (78%) and has not been officially endorsed by the ACR.

III. While not entirely clear at this time what long-term effects tocilizumab use has on the underlying pathophysiology and outcomes in giant cell arteritis patients, treatment to maintain remission may prevent potential adverse effects associated with long-term glucocorticoid use. A large proportion of patients, however, will not have return/relapse of giant cell arteritis after a successful taper of prednisone over one to two years, and in most cases relapses do not lead to major adverse effects such as vision loss. Glucocorticoids are thus considered standard of care as first-line therapy and the primary treatment in patients presenting with giant cell arteritis. A guideline published by the British Society for Rheumatology (BSR)/British Health Professional in Rheumatology (BHPR) recommends that adjuvant therapy with methotrexate or other immunosuppressants be considered with recurrent relapses (started at the third relapse) or in patients who are unsuccessful with glucocorticoid taper.

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Cryopyrin-Associated Periodic Syndromes (CAPS)

Initial Evaluation

I. **Anakinra (Kineret)** may be considered medically necessary when the following criteria below are met:
   A. Member is being managed by or in consultation with a rheumatologist; **AND**

B. A diagnosis of a **cryopyrin-associated periodic syndrome (CAPS), including neonatal-onset multisystem inflammatory disease (NOMID), familial cold autoinflammatory syndrome (FCAS) or Muckle-Wells syndrome (MWS); AND**
C. Member has documented laboratory evidence of a genetic mutation in the Cold-Induced Auto-inflammatory Syndrome 1 (CIAS1), also known as NLRP

II. **Rilonacept (Arcalyst)** may be considered medically necessary when the following criteria below are met:
A. Member is 12 years of age or older; **AND**
B. Member is being managed by or in consultation with a rheumatologist; **AND**
C. A diagnosis of **CAPS, including FCAS or MWS**; **AND**
D. Member has documented laboratory evidence of a genetic mutation in the Cold-Induced Auto-inflammatory Syndrome 1 (CIAS1), also known as NLRP3

Renewal Evaluation

I. Member has exhibited improvement or stability of disease symptoms; **AND**
II. Agent prescribed will not be used in combination with other biologics or other non-biologic specialty medication used to treat psoriatic arthritis or another auto-immune condition (e.g. Otezla, Xeljanz, Olumiant)

Supporting Evidence

I. Anakinra (Kineret) is FDA approved for the treatment of CAPS, particularly neonatal-onset multisystem inflammatory disease (NOMID). Anakinra is also frequently employed in the other CAPS, including Muckle-Wells syndrome (MWS) and familial cold autoinflammatory syndrome (FCAS), and can lead to rapid symptom improvement and a decrease in inflammatory markers. The pivotal trial in patients with NOMID was a single arm, prospective study that examined 43 patients treated with anakinra for up to 60 months. Outcomes included the use of a disease-specific symptom diary as well as reduction in inflammatory markers, with improvement seen in both. Eleven patients also went through a withdrawal phase, in which symptoms/inflammatory markers worsened, followed by response again when anakinra was reinitiated. A retrospective review of 22 patients with CAPS (varied phenotypes), demonstrated efficacy of anakinra. All 15 patients treated with anakinra achieved serologic remission and resolution of symptoms (fever, rash, conjunctivitis, and rheumatic symptoms). Other small, observational studies have demonstrated similar improvements both serologically and symptomatically in patients with MWS and FCAS.
II. Rilonacept (Arcalyst) is FDA approved for treatment of CAPS, particularly in patients 12 years of age and older with familial cold autoinflammatory syndrome (FCAS) or Muckle-Wells syndrome (MWS). The relevant phase III trials included 47 patients who were randomized to either weekly rilonacept or placebo, with the first trial analyzing efficacy within a six-week follow-up, and the

second looking at response after withdrawal of the agent in the same population. Disease activity via symptom score (0-10 scale) was significantly reduced within a few days of onset (84% rilonacept vs 13% placebo), with a decrease in inflammatory markers also observed. No data is available for analysis in the NOMID population, and no head-to-head comparison with anakinra have been identified at this time.

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Investigational or Not Medically Necessary Uses

I. Atopic Dermatitis
   A. Early report from the BREEZE-AD1 and BREEZE-AD2 studies have indicated that baricitinib may be beneficial in patients with atopic dermatitis. The manufacturer reports a statistical improvement in Investigator's Global Assessment (IGA) scores at week 16 compared to placebo, though full trial data and outcomes has not been shared at this point in time. Three other studies are also planned which may provide data on safety and efficacy as well.

II. Cutaneous Sarcoidosis
   A. Apremilast and adalimumab have both been analyzed in this disease state. Efficacy data is limited to case reports and small studies at this time. One small RCT of adalimumab (n = 16) demonstrated a decrease in target lesion area compared to placebo. Similarly, a small observational study in 15 patients receiving apremilast demonstrated a reduction in induration at week 12 compared to baseline. Only one investigator performed the lesion assessment in this study, and similar to adalimumab, further larger scale, randomized studies are needed to fully establish efficacy of these agents.

III. Familial Mediterranean Fever
   A. Current studies for Familial Mediterranean Fever, a subgroup of periodic fever syndrome, are limited to case reports. In evaluating current evidence available, quantitative evaluation of response to biologic treatments (e.g. tocilizumab, infliximab, etanercept,

adalimumab, anakinra and canakinumab) is difficult to obtain, and therefore, difficult to assess true efficacy and safety. In the absence of controlled studies to evaluate the safety and efficacy of biologics in the treatment of patients with Familial Mediterranean Fever, the use of biologics in this setting would be considered experimental and investigational.

IV. Graft Versus Host Disease (GVHD)
    A. A number of observational trials have examined etanercept in acute GVHD. Treatment regimens vary significantly between these observational studies. Data from a pilot and phase II trial pooled against observational data of standard of care patients receiving standard of care with steroids observed a higher complete response rate in those treated with etanercept. The results are significantly limited, however, by the observational, nonrandomized nature and thus prospective, randomized trials are needed to fully establish possible benefit in GVHD. The use of tocilizumab has also been studied in a small population (n = 8) with refractory GVHD. While response was observed in four of the six tocilizumab treated patients, the limited sample size is insufficient to confirm efficacy at this time.
V. Grave's Ophthalmopathy
    A. A small, phase III RCT (n = 32) analyzed tocilizumab use compared to placebo in this disease state. A statistically significant reduction was observed in the clinical activity score from baseline by week 16, but given the small sample size, the American Academy of Ophthalmology has recommended that larger studies be completed to fully establish safety and efficacy for this indication.
VI. Guttate Psoriasis
    A. In this form of psoriasis, case reports suggest that the use of TNF inhibitors may induce flares when used. Typical treatment involves phototherapy and topical corticosteroids/vitamin D analogs, with tonsillectomy or antibiotics used for more refractory disease. There is no established efficacy data for the use of biologics or targeted DMARDs in this setting at this time.
VII. Interstitial Cystitis
    A. TNF inhibitors such as adalimumab and certolizumab pegol have been studied in small, phase III RCTs. In the study of certolizumab pegol, no difference was observed in interstitial cystitis compared to placebo at week 2. Secondary outcomes indicate benefit may occur in this population by week 10-18 of therapy. A similar study was completed with adalimumab, with no statistical difference observed in the primary outcome at week 12 compared to placebo. Further studies are needed to analyze efficacy in this population.
VIII. Lupus Nephritis and Systemic Lupus Erythematosus (SLE)
    A. Abatacept was analyzed in a large phase III RCT (n =695) in patients with lupus nephritis and in combination with mycophenolate and steroids. No difference was observed in the

primary outcome of complete renal response at one year compared to placebo. Studies utilizing baricitinib and ustekinumab are currently recruiting in patients with SLE.

IX. Osteoarthritis
    A. Infliximab and adalimumab have been examined for use in patients with erosive, hand osteoarthritis. Mixed results have been seen so far. Open-label, observational studies of infliximab have shown potential benefit, while studies with adalimumab have been inconclusive. For instance, in a RCT of 60 patients, the difference in proportion of active disease in the adalimumab versus placebo group was not statistically significant. Further studies are needed to establish safety and efficacy.
X. Palmoplantaris Pustulosis
    A. A small placebo-controlled (n =15) of etanercept in palmoplantaris pustolosis supported potential efficacy of TNF inhibitors. Observations have also occurred demonstrating worsening of this disease with use of TNF inhibitors. Other biologics, such as the use of IL-12/IL-23 inhibitor ustekinumab, did not demonstrate benefit in palmoplantaris pustolosis. A phase II study has analyzed guselkumab, and case reports of IL-1 inhibitors such as anakinra have been reported, though further study is needed to confirm the use of biologics in this population.
XI. Polymyalgia Rheumatica
    A. A phase III placebo-controlled study (n = 40) of etanercept demonstrated mild reduction in disease severity scores, though the response was only analyzed at two weeks. The TNF inhibitor infliximab was also examined in a RCT (n = 51). No statistical difference was observed in relapse between the infliximab and standard of care groups. A phase III study is currently recruiting looking at the IL-6 inhibitors tocilizumab and sarilumab use in this population.
XII. Polymyositis and Dermatomyositis
    A. One phase III trial is currently recruiting to analyze abatacept in patients with polymyositis and dermatomyositis. Anakinra has also been examined in a single group study (n = 15). Decrease in certain inflammatory markers was observed, however, the clinical and patient-centered outcomes of anakinra use in this population requires further analysis. Another single-group, non-randomized trial (n = 13) looked at infliximab use in this population. None of the included patients had improvement in muscle strength by manual, and only two patients saw any improvement in disease activity scores.
XIII. Pulmonary Sarcoidosis
    A. The TNF inhibitors infliximab, adalimumab, and etanercept have been studied to some extent in pulmonary sarcoidosis. A phase II study (n = 138) saw a statistically significant increase in functional vital capacity at week 24 compared to placebo, however, the effect size was small with a mean increase of just 2.5% from baseline. A small, open-label phase II study with etanercept was terminated early due to an excessive number of treatment failures. Case reports of adalimumab exist, and one study which examined 18 patients

who switched after infliximab use saw improvement in just over one-third of patients, however, further prospective, randomized trials would be needed to fully establish safety and efficacy.

XIV. Pyoderma gangrenosum
   A. Case reports of the use of TNF inhibitors are available in this patient population. Most reports have involved patients with another indication for a TNF inhibitor, such as IBD or RA. A Phase III trial for this disease state is currently recruiting in Japan.

XV. Sciatica
   A. One small RCT has examined adalimumab in patients with acute/severe radicular leg pain and imagine-confirmed lumber disc herniation. Of the 61 patients, a statistically significant, though small effect, was seen at week 6 compared to placebo. At the 6 month follow up, the statistically significant difference was lost. While a difference in surgical discectomies was also seen,

XVI. Systemic sclerosis (scleroderma)
   A. A phase III RCT (n =212) comparing tocilizumab to placebo in patients with systemic sclerosis did not observe a statistically significant difference in change from baseline to week 48 in the primary outcome in the Modified Rodnan Skin Score (mRSS).

XVII. Sjogren's Syndrome
   A. Studies with TNF inhibitors etanercept and infliximab have not demonstrated benefit in Sjogren's syndrome. A RCT (n = 103) found no difference in disease activity between infliximab and placebo by week 22. Likewise, a smaller RCT (n = 28) found no statistical difference with etanercept versus placebo at 12 weeks after treatment initiation. Small, open-label studies have also been done with abatacept, though sample size has been small and data has been mixed, with one trial demonstrating improvement in salivary gland biopsy and extraglandular manifestations, and one showing no change in tear flow or improvement in other symptoms.

XVIII. Wegener's Granulomatosis
   A. One phase III RCT (n = 181) exists for the use of etanercept in patients with Wegener's Granulomatosis. Compared to standard of care (steroids plus cyclophosphamide or methotrexate), patient on etanercept demonstrated an initial sustained remission for at least six months that was not statistically different from standard of care. Likewise, a large proportion of patients lost response over the 27 month mean follow up period. An open-label study with infliximab (n = 16) has also been completed, with similar response rates to that described above in the etanercept study.

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Policy Implementation/Update:

Action and Summary of Changes	Date
Updated PA policy to include FDA approvals for Stelara and Taltz for plaque psoriasis in pediatric population. Updated supporting information section for plaque psoriasis to include clinical trial data supporting use of Stelara and Taltz in pediatric patients	09/2020
Updated the products for psoriatic arthritis to include guselkumab (Tremfya). Updated the supporting evidence section for psoriatic arthritis to reflect no changes in the guidelines with regard to guselkumab (Tremfya). Updated non-radiographic axial spondyloarthritis (nr-axSpA) criteria to include secukinumab (Cosentyx) and ixekizumab (Taltz). Updated nr-axSpA supporting evidence section to include trial information regarding new addition of secukinumab (Cosentyx) and ixekizumab (Taltz), as well as updated ACR guidelines.	08/2020
Removed Behçet syndrome from the E/I Section	02/2020
<u>Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis</u> • Added ixekizumab (Taltz) per new FDA indication <u>Cryopyrin-Associated Periodic Syndromes (CAPS)</u> • Added E/I information regarding Familial Mediterranean Fever <u>Ulcerative Colitis</u> • Added ustekinumab (Stelara) per FDA indication	11/2019

Criteria updated to new policy format. Specific changes include:
Rheumatoid Arthritis
• Removed the number of joints and duration of disease question as evidence and guidelines did not support the requirement
• Removed requirements for diagnosis due to varying methods to diagnose and limited value of this question from health plan standpoint
• Clarified use of oral DMARD requirement may be bypassed if all of them are contraindicated
• Added newly approved upadacitinib (Rinvoq) as a non-preferred alternative
Polyarticular Juvenile Idiopathic Arthritis (PJIA)
• Removed the number of joints and duration of disease question as evidence and guidelines did not support the requirement
• Added route to approval of Actemra as Actemra was previously in a separate policy
Systemic Juvenile Idiopathic Arthritis (SJIA)
• Separated SJIA from PJIA to have individual requirements
• Removed the number of joints and duration of disease question as evidence and guidelines did not support the requirement
• Updated route to approval to require trial of NSAIDs or indication member has severe active disease
• Routed therapy through anakinra (Kineret) over tocilizumab (Actemra) and abatacept (Orencia); followed by tocilizumab (Actemra) over abatacept (Orencia) as per
Psoriatic Arthritis
• Added requirement of the presence of active severe disease and provided specific indicators of severe disease
• Added clinical note: "If a patient has a diagnosis of both plaque psoriasis and psoriatic arthritis, approval of the requested medication can be made as long as the patient fulfills the criteria for at least one of the disease states and associated medication criteria."
Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis
• Removal of the requirement of DMARDs per the 2015 ACR guideline and 2016 ASAS/EULAR guideline
• Added requirement of a trial of two or more NSAIDS for an adequate trial of at least 4 weeks, also based on the above guidelines
• Added ixekizumab (Taltz) per new FDA indication
Plaque Psoriasis
• Clarified that moderate to severe disease is needed for payment consideration
• Clarified use of oral DMARD requirement may be bypassed if all are contraindicated
Crohn's Disease
• Added age requirement of six years of age or older
• Incorporated definition of moderate to severe Crohn's disease to help confirm disease severity
• Addition of breakdown to separate severe/fulminant Crohn's disease with definition to help confirm disease severity
  ○ Addition of IV corticosteroids as appropriate for this level of severity
• Addition of breakdown to Crohn's disease with surgical resection completed or planned
  ○ With further addition requiring presence of one additional factor demonstrating medical necessity of biologic treatment
Ulcerative Colitis
	08/2019

• Added age of 18 years or older • Addition of trial of thiopurine for at least 8 weeks • Added ustekinumab (Stelara) per FDA indication <u>Behcet's Disease</u> • New indication added following approval of Otezla in this setting • Literature supports TNF therapy in oral and ophthalmic manifestations for Bechet's. A path to approval was added to the criteria • Otezla was added as a potential option after TNF have been found inefficacious or are contraindicated <u>Hidradentitis Suppurativa</u> • Updated prescriber language to be consistent with other sections • Added requirement of a trial of antibiotics for moderate disease <u>Uveitis/Panuveitis</u> • Added age of 2 years or older • Improved trial/fail wording to state "ineffective, contraindicated, or not tolerated" o No changes to trial and failure requirements <u>Giant Cell Arteritis (GCA)</u> • Added age of 18 years or older • Added criteria endorsed by guidelines to confirm diagnosis of GCA • Updated terminology around steroid use to require a previous trial with steroids rather than requiring concomitant steroid use with Actemra <u>Cryopyrin-Associated Periodic Syndromes (CAPS)</u> • Added requirement, of documented laboratory evidence of a genetic mutation	
Updated criteria to require trial and failure of Enbrel, Humira AND Cosentyx for Plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis	11/2018
Criteria update: Increased initial approval from 3 months to 6 months, updated initial QL to reflect 6 month approval duration. Added new Xeljanz IR 10mg tablet availability. Added baricitinib (Olumiant) as an option for the treatment of rheumatoid arthritis after trial and failure of a TNF antagonist.	07/2018
Criteria update: Added new Kevzara auto injector formulation, Xeljanz new indication in ulcerative colitis, added Cimzia new indication in plaque psoriasis, minor formatting edits.	06/2018
Criteria update: Align dosage and administration with quantity limit. Removal of the question pertaining to active infection.	02/2018
New Criteria Set – consolidated from all biologic agents along with Otezla and Xeljanz criteria sets. Within this new criteria set, here are the following updates: 1. 18 years of age requirement has been removed for Stelara as it has now been FDA approved for pediatric plaque psoriasis. 2. New FDA approved indication of psoriatic arthritis has been added for Xeljanz/Xeljanz XR and Taltz 3. The question regarding dual therapy has been refined to encompass the language of biologics and other non-biologics (e.g. Otezla and Xeljanz). 4. The question regarding DMARDs has been refined to only include agents that are administered non-biologic, non-specialty and that are administered orally. 5. For the indication of plaque psoriasis, the question addressing the trial of UVB has been combined with the trial of DMARDs.	01/2018