Title: Immune Modulating Therapies for Rheumatologic, Dermatologic and Gastrointestinal Diseases

Policy #: Rx.01.154

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **abatacept (Orencia® SQ), adalimumab (Humira®), anakinra (Kineret®), apremilast (Otezla®), certolizumab (Cimzia®), etanercept (Enbrel®), golimumab (Simponi®), secukinumab (Cosentyx®), tocilizumab (Actemra SQ®), tofacitinib (Xeljanz [XR]®), methotrexate injection (Otrexup®, Rasuvo®, Reditrex™), ustekinumab (Stelara®), ixekizumab (Taltz®), sarilumab (Kevzara®), brodalumab (Siliq™), rilonacept (Arcalyst®), baricitinib (Olumiant®), guselkumab (Tremfya®), risankizumab-rzaa (Skyrizi™), and Upadacitinib (Rinvoq™)** as provided under the member's prescription drug benefit.

Description:

Abatacept (Orencia® SQ) is a selective costimulation modulator, inhibits T-cell (T-lymphocyte) activation by binding to CD80 and CD86, thereby blocking interaction with CD28. This interaction provides a costimulatory signal necessary for full activation of T-lymphocytes. Activated T-lymphocytes are implicated in the pathogenesis of RA and are found in the synovium of patients with RA.

Adalimumab (Humira®) is a recombinant human immunoglobulin G1 (IgG1) monoclonal antibody, which binds specifically to TNF-alpha and blocks its interaction with the p55 and p75 cell surface TNF receptors. Adalimumab also lyses surface TNF-expressing cells in vitro in the presence of a complement. Adalimumab does not bind or inactivate lymphotoxin (TNF-beta). Adalimumab also modulates biological responses that are induced or regulated by TNF, including changes in the levels of adhesion molecules responsible for leukocyte migration (ELAM-1, VCAM-1, and ICAM-1 with a 50% inhibitory concentration of 1 to 2×10^{-10}M).

Anakinra (Kineret®) is a recombinant, nonglycosylated form of the human interleukin-1 receptor antagonist (IL-1Ra). It blocks the biologic activity of IL-1 alpha and beta by competitively inhibiting IL-1 binding to the IL-1RI, which is expressed in a wide variety of tissues and organs.

Apremilast (Otezla®) inhibits phosphodiesterase 4 (PDE4) specific for cyclic adenosine monophosphate (cAMP) which results in increased intracellular cAMP levels and regulation of numerous inflammatory mediators (e.g., decreased expression of nitric oxide synthase, TNF-alpha, and interleukin [IL]-23, as well as increased IL-10).

Baricitinib (Olumiant®) is a Janus Kinase (JAK) inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Within the signaling pathway, JAKs phosphorylate and activate Signal Transducers and Activators of Transcription (STATs) which modulate intracellular activity including gene expression. Baricitinib modulates the signaling pathway at the point of JAKs, preventing the phosphorylation and activation of STATs.

Certolizumab (Cimzia®) is a pegylated humanized antibody Fab. fragment of tumor necrosis factor alpha (TNF-alpha) monoclonal antibody. Certolizumab pegol binds to and selectively neutralizes human TNF-alpha activity.

Etanercept (Enbrel®) is a dimeric soluble form of the p75 TNFR that can bind TNF molecules. Etanercept inhibits binding of TNF-alpha and TNF-beta (lymphotoxin alpha) to cell surface TNFRs, rendering TNF biologically inactive. In in vitro studies, large complexes of etanercept with TNF-alpha were not detected, and cells expressing transmembrane TNF that binds etanercept are not lysed in the presence or absence of complement

Golimumab (Simponi®) is a human monoclonal antibody that binds to both the soluble and transmembrane bioactive forms of human TNF-alpha. This interaction prevents the binding of TNF-alpha to its receptors, thereby inhibiting the biological activity of TNF-alpha (a cytokine protein).

Guselkumab (Tremfya®) is a human monoclonal IgG1gamma antibody that binds to interleukin-23 (IL-23) and inhibits the interaction with its receptor blocker. IL-23 is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Guselkumab inhibits the release of proinflammatory cytokines and chemokines

Ixekizumab (Taltz®) is a humanized IgG4 monoclonal antibody that selectively binds with the interleukin 17A (IL-17A) cytokine and inhibits its interaction with the IL-17 receptor. IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Ixekizumab inhibits the release of proinflammatory cytokines and chemokines.

Rilonacept (Arcalyst®) is an interleukin-1 blocker which blocks IL-1β signaling by acting as a soluble decoy receptor that binds IL-1β and prevents its interaction with cell surface receptors. Rilonacept also binds IL-1α and IL-1 receptor antagonist (IL-1ra) with reduced affinity.

Risankizumab-rzaa (Skyrizi™) is a humanized immunoglobulin G1 (IgG1) monoclonal antibody that selectively binds to the p19 subunit of human interleukin 23 (IL-21) cytokine and inhibits its interaction with the IL-23 receptor. IL-23 is a naturally occurring cytokine that is involved in inflammatory and immune responses. Risankizumab-rzaa inhibits the release of pro-inflammatory cytokines and chemokines.

Sarilumab (Kevzara®) is a human recombinant IgG1 monoclonal antibody that binds to the IL-6 receptor and has been shown to inhibit IL-6-mediated signaling through these receptors. IL-6 has been shown to be involved in a variety of inflammatory processes.

Secukinumab (Cosentyx®) is a human IgG1 monoclonal antibody that selectively binds to interleukin-17A (IL-17A) cytokine and inhibits its interaction with the IL-17 receptor. IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Secukinumab inhibits the release of proinflammatory cytokines and chemokines.

Tocilizumab (Actemra® SQ) is an antagontist of the interleukin-6 (IL-6) receptor. Endogenous IL-6 is induced by inflammatory stimuli and mediates a variety of immunological responses. Inhibition of IL-6 receptors by tocilizumab leads to a reduction in cytokine and acute phase reactant production.

Tofacitinib (Xeljanz®[XR]) inhibits Janus kinase (JAK) enzymes, which are intracellular enzymes involved in stimulating hematopoiesis and immune cell function through a signaling pathway. In response to extracellular cytokine or growth factor signaling, JAKs activate signal transducers and activators of transcription (STATs), which regulate gene expression and intracellular activity. Inhibition of JAKs prevents cytokine- or growth factor–mediated gene expression and intracellular activity of immune cells, reduces circulating CD16/56+ natural killer cells, serum IgG, IgM, IgA, and C-reactive protein, and increases B cells.

Ustekinumab (Stelara®) disrupts IL-12 and IL-23 mediated signaling and cytokine cascades.

Upadacitinib (Rinvoq™) is a Janus kinase (JAK) inhibitor. JAKs are intracellular enzymes which transmit signals arising from cytokine or growth factor-receptor interactions on the cellular membrane to influence cellular processes of hematopoiesis and immune cell function. Within the signaling pathway, JAKs phosphorylate and activate Signal Transducers and Activators of Transcription (STATs) which modulate intracellular activity including gene expression. Upadacitinib modulates the signaling pathway at the point of JAKs, preventing the phosphorylation and activation of STATs. JAK enzymes transmit cytokine signaling through their pairing (e.g., JAK1/JAK2, JAK1/JAK3, JAK1/TYK2, JAK2/JAK2, JAK2/TYK2). In a cell-free isolated enzyme assay, upadacitinib had greater inhibitory potency at JAK1 and JAK2 relative to JAK3 and TYK2. In human leukocyte cellular assays, upadacitinib inhibited cytokine-induced STAT phosphorylation mediated by JAK1 and JAK1/JAK3 more potently than JAK2/JAK2 mediated STAT phosphorylation. However, the relevance of inhibition of specific JAK enzymes to therapeutic effectiveness is not currently known

Methotrexate injection (Otrexup™, Rasuvo®, Reditrex™) inhibits dihydrofolic acid reductase. Dihydrofolates must be reduced to tetrahydrofolates by this enzyme before they can be utilized as carriers of 1-carbon groups in the synthesis of purine nucleotides and thymidylate. Therefore, methotrexate interferes with DNA synthesis, repair, and cellular replication. Actively proliferating tissues such as malignant cells, bone marrow, fetal cells, buccal and intestinal mucosa, and cells of the urinary bladder are in general more sensitive to this effect of methotrexate. When cellular proliferation in malignant tissues is greater than in most normal tissues, methotrexate may impair malignant growth without irreversible damage to healthy tissues.
The mechanism of action in RA is unknown; it may affect immune function.
In psoriasis, the rate of production of epithelial cells in the skin is greatly increased over normal skin. This differential in proliferation rates is the basis for the use of methotrexate to control the psoriatic process.

Methotrexate injection/vial (Otrexup™, Rasuvo®, Reditrex™) are eligible for coverage under both pharmacy and medical benefit.

Summary Tables

Table 1: Non-biologics

INDICATION/	AS	CD	NOMID/CAPS	PP	PJIA	PA	RA	SJIA	UC	Behcet's Syndrome

AGENT										
Otelza® (apremilast)				X		X				X
Methotrexate injection (i.e Otrexup®, Rasuvo®, Reditrex™)		X		X	X		X			

Table 2: Non-Tumor Necrosis Factor (TNF) Biologics

INDICATION/ AGENT	AS	CD	NOMID	PP	PJIA	PA	RA	SJIA	UC	GCA	CAPS/ FCAS/MWS	nr-axSpA	DIRA	SSc-ILD	Recurrent pericarditis
Actemra ® (tocilizumab)					X		X	X		X				x	
Stelara® (ustekinumab)		X		X		X			X						
Cosentyx® (secukinumab)	X			X		X						X			
Taltz® (ixekizumab)				X		X						X			
Kineret ® (anakinra)			X				X						X		
Orencia ® SQ (abatacept)					X	X	X								
Xeljanz ® [XR] (tofacitinib)					X	X	X		X						
Kevzara ® (sarilumab)							X								
Siliq™ (brodalumab)				X											
Tremfya® (guselkumab)				X		X									
Olumiant® (baricitinib)							X								
Arcalyst® (rilonacept)											X		X		x
Skyrizi™ (risankizumab-rzaa)				X											
Rinvoq™(upadacitinib)							X								

Table 3: Anti-TNF Biologics

INDICATION/ AGENT	AS	CD	HS	NOMID/CAPS	PP	PJIA	PA	RA	SJIA	UC	Uveitis	nr-axSpA
Cimzia® (certolizumab)	X	X			X		X	X				X (with objective signs of inflamm-ation)
Enbrel (etanercept)	X				X (starting at age 4)	X (aged 2 years or older)	X	X				
Humira (adalimumab)	X	X	X		X	X	X	X		X	X	
Simponi (golimumab)	X						X	X		X		

Legend

ACRONYM	**INDICATION**
AS	Ankylosing Spondylitis
CD	Crohn's Disease
NOMID/CAPS	Neonatal-onset Multisystem Inflammatory Disease/ Cryopyrin-Associated Periodic Syndromes
PP	Plaque Psoriasis
PJIA	Polyarticular Juvenile Idiopathic Arthritis
PA	Psoriatic Arthritis
RA	Rheumatoid Arthritis
SJIA	Systemic Juvenile Idiopathic Arthritis
UC	Ulcerative Colitis
HS	Hidradenitis Suppurativa
GCA	Giant Cell Arteritis
CAPS/ FCAS/ MWS	Cryopyrin-Associated Periodic Syndromes Familial cold Auto-Inflammatory Syndrome (FCAS) and/or Muckle-Wells Syndrome (MWS)

DIRA	Deficiency of Interleukin-1 Receptor Antagonist
nr-axSpA	Non-radiographic Axial Spondyloarthritis
SSc-ILD	Systemic sclerosis-associated interstitial lung disease

Policy:

Rheumatoid Arthritis (RA)

INITIAL CRITERIA Adalimumab (Humira®), certolizumab (Cimzia®), golimumab (Simponi®), tofacitinib (Xeljanz [XR]® tablets/extended-release tablets) or upadacitinib (Rinvoq™) is approved when there is a diagnosis of moderate to severe RA and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a rheumatologist; and
3. Member had inadequate response of inability to tolerate ONE of the following disease-modifying anti-rheumatic drugs (DMARDS): methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA Anakinra (Kineret®), etanercept (Enbrel®), sarilumab (Kevzara®), baricitinib (Olumiant®) is approved when there is a diagnosis of moderate to severe RA and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a rheumatologist; and
3. ONE of the following:
    a. Both of the following:
        i. Inadequate response or inability to tolerate TWO of the following: adalimumab (Humira®), certolizumab (Cimzia®), golimumab (Simponi®) tofacitinib (Xeljanz [XR]® tablets/extended-release tablets) or upadacitinib (Rinvoq™); and
        ii. Inadequate response or inability to tolerate BOTH of the following: abatacept (Orencia® SQ) and tocilizumab (Actemra® SQ); or
    b. Continuation of therapy with the requested product; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA Abatacept (Orencia® SQ) or tocilizumab (Actemra® SQ) is approved when there is a diagnosis of moderate to severe RA and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a rheumatologist; and
3. One of the following:
    a. Inadequate response or inability to tolerate TWO of the following: adalimumab (Humira®), certolizumab (Cimzia®), golimumab (Simponi®), tofacitinib (Xeljanz [XR]® tablets/extended-release tablets) or upadacitinib (Rinvoq™) ; or
    b. Continuation of therapy with the requested product; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA: Methotrexate injection (i.e., Otrexup™, Rasuvo®, Reditrex™) is approved when there is diagnosis of severe, active rheumatoid arthritis (RA) and ALL of the following:

1. Recommended by a rheumatologist; and
2. Inadequate response or inability to tolerate oral methotrexate; and
3. For Otrexup™ and Reditrex™ only: inadequate response or inability to tolerate Rasuvo®

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Adalimumab (Humira®), certolizumab (Cimzia®), golimumab (Simponi®), tofacitinib (Xeljanz [XR]® tablets/extended-release tablets), upadacitinib (Rinvoq™), anakinra (Kineret®), etanercept (Enbrel®), sarilumab (Kevzara®), baricitinib (Olumiant®), abatacept (Orencia® SQ), tocilizumab (Actemra® SQ), or methotrexate injection (i.e., Otrexup™, Rasuvo®, Reditrex™) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Ankylosing Spondylitis (AS)

INITIAL CRITERIA: Adalimumab (Humira®), certolizumab (Cimzia®), or golimumab (Simponi®) is approved when there is a diagnosis of AS and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a rheumatologist; and
3. Member had inadequate response or inability to tolerate two NSAIDS; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA Etanercept (Enbrel®) or secukinumab (Cosentyx®) is approved when there is a diagnosis or active AS and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a rheumatologist; and
3. One of the following:
    a. Both of the following:
        i. Inadequate response or inability to tolerate TWO of the following: adalimumab (Humira®), certolizumab (Cimzia®), or golimumab (Simponi®); and
        ii. Inadequate response or inability to tolerate ixeckizumab (Taltz®); or
    b. Continuation of therapy with the requested product; and
    c. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA: Ixekizumab (Taltz®) is approved when there is a diagnosis of active AS and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a rheumatologist; and
3. One of the following:
    a. Inadequate response or inability to tolerate ONE of the following: adalimumab (Humira®), certolizumab (Cimzia®) or golimumab (Simponi®); or
    b. Continuation of therapy with the requested product; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Adalimumab (Humira®), certolizumab (Cimzia®), golimumab (Simponi®), Etanercept (Enbrel®), secukinumab (Cosentyx®), or ixekizumab (Taltz®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Polyarticular Juvenile Idiopathic Arthritic (PJIA)

INITIAL CRITERIA: Adalimumab (Humira®) is approved when there is a diagnosis of moderate to severe PJIA and ALL of the following:

1. Member is 2 years of age or older; and
2. Recommended by a rheumatologist; and
3. Inadequate response or inability to tolerate ONE of the following DMARDs: methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA: Tocilizumab (Actemra® SQ), abatacept (Orencia® SQ), tofacitinib (Xeljanz® tablets and oral solution) is approved when there is a diagnosis of moderate to severe PJIA and ALL of the following:

1. Member is 2 years of age or older; and
2. Recommended by a rheumatologist; and
3. One of the following:
    a. Inadequate response or inability to tolerate adalimumab (Humira®); or
    b. Continuation of therapy with the requested product;
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA: Etanercept (Enbrel®) is approved when there is a diagnosis of moderate to severe PJIA and ALL of the following:

1. Member is 2 years of age or older; and
2. Recommended by a rheumatologist; and

3. One of the following:
    a. Inadequate response or inability to tolerate ALL of the following: adalimumab (Humira®), tocilizumab (Actemra® SQ), tofacitinib (Xeljanz® tablets and oral solution) and abatacept (Orencia® SQ); or
    b. Continuation of therapy with the requested product;
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA: Methotrexate injection (i.e. Otrexup™, Rasuvo®, Reditrex™) is approved when there is diagnosis of polyarticular juvenile idiopathic arthritis (pJIA) and ALL of the following:

1. Recommended by a rheumatologist; and
2. Inadequate response or inability to tolerate oral methotrexate; and
3. For Otrexup™ and Reditrex™ only: inadequate response or inability to tolerate Rasuvo®

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Adalimumab (Humira®), Tocilizumab (Actemra® SQ), abatacept (Orencia® SQ), tofacitinib (Xeljanz® tablets and oral solution), etanercept (Enbrel®), or methotrexate injection (i.e., Otrexup™, Rasuvo®, Reditrex™) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Psoriatic Arthritis

INITIAL CRITERIA: Adalimumab (Humira®), certolizumab (Cimzia®), ustekinumab (Stelara®), apremilast (Otezla®), golimumab (Simponi®), or guselkumab (Tremfya®) is approved when there is a diagnosis of moderate to severe psoriatic arthritis and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a rheumatologist or dermatologist; and
3. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA: Abatacept (Orencia® SQ) or tofacitinib (Xeljanz®/Xeljanz® XR tablets/extended-release tablets) is approved when there is a diagnosis of moderate to severe psoriatic arthritis and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a rheumatologist or dermatologist; and
3. One of the following:
    a. Inadequate response or inability to tolerate TWO of the following: adalimumab (Humira®), certolizumab (Cimzia®), ustekinumab (Stelara®), golimumab (Simponi®), or guselkumab (Tremfya®); or
    b. Continuation of therapy with the requested product;
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA: Ixekizumab (Taltz®) is approved when there is a diagnosis of moderate to severe psoriatic arthritis and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a rheumatologist or dermatologist; and
3. One of the following:
    a. Inadequate response or inability to tolerate ONE of the following: adalimumab (Humira®), certolizumab (Cimzia®), ustekinumab (Stelara®), golimumab (Simponi®), or guselkumab (Tremfya®); or
    b. Continuation of therapy with the requested product; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA Etanercept (Enbrel®) is approved when there is a diagnosis of moderate to severe psoriatic arthritis and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a rheumatologist or dermatologist; and
3. One of the following:
    a. Both of the following:
        i. Inadequate response or inability to tolerate TWO of the following: adalimumab (Humira®), certolizumab (Cimzia®), golimumab (Simponi®), ustekinumab (Stelara®), or guselkumab (Tremfya®); and

ii. Inadequate response or inability to tolerate TWO of the following: abatacept (Orencia® SQ), tofacitinib (Xeljanz®/Xeljanz® XR tablets/extended-release tablets) or ixekizumab (Taltz®); or
b. Continuation of therapy with the requested product; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA: Secukinumab (Cosentyx®) is approved when there is a diagnosis of moderate to severe psoriatic arthritis and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a rheumatologist or dermatologist; and
3. One of the following:
   a. All of the following:
      i. Inadequate response or inability to tolerate TWO of the following: adalimumab (Humira®), certolizumab (Cimzia®), golimumab (Simponi®), ustekinumab (Stelara®), or guselkumab (Tremfya®); and
      ii. Inadequate response or inability to tolerate ixekizumab (Taltz®); and
      iii. Inadequate response or inability to tolerate ONE of the following: abatacept (Orencia® SQ) or tofacitinib (Xeljanz®/Xeljanz® XR tablets/extended-release tablets); or
   b. Continuation of therapy with the requested product; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA: Methotrexate injection (i.e., Otrexup®, Rasuvo®, Reditrex™) is approved when there is diagnosis of psoriatic arthritis (PsA) and ALL of the following:

1. Recommended by a rheumatologist or dermatologist; and
2. Inadequate response or inability to tolerate oral methotrexate; and
3. For Otrexup™ and Reditrex™ only: inadequate response or inability to tolerate Rasuvo®

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Adalimumab (Humira®), certolizumab (Cimzia®), ustekinumab (Stelara®), apremilast (Otezla®), golimumab (Simponi®), guselkumab (Tremfya®), abatacept (Orencia® SQ), tofacitinib (Xeljanz®/Xeljanz® XR tablets/extended-release tablets), Ixekizumab (Taltz®), etanercept (Enbrel®), secukinumab (Cosentyx®), or methotrexate injection (i.e., Otrexup®, Rasuvo®, Reditrex™) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Plaque Psoriasis

INITIAL CRITERIA: Adalimumab (Humira®), guselkumab (Tremfya®), certolizumab (Cimzia®), risankizumab (Skyrizi™) or apremilast (Otezla®) is approved when there is a diagnosis of moderate to severe chronic plaque psoriasis and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a dermatologist; and
3. Member had inadequate response of inability to tolerate ONE of the following: topical calcipotriene containing products, topical anthralin, topical steroids, topical immune modulators (Elidel®, Protopic®), topical retinoids; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA: Ustekinumab (Stelara®) is approved when there is a diagnosis of moderate to severe chronic plaque psoriasis and ALL of the following:

1. Member is 6 years of age or older; and
2. Recommended by a dermatologist; and
3. Member had inadequate response of inability to tolerate ONE of the following: topical calcipotriene containing products, topical anthralin, topical steroids, topical immune modulators (Elidel®, Protopic®), topical retinoids; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA Secukinumab (Cosentyx™) is approved when there is diagnosis of moderate to severe chronic plaque psoriasis and ALL of the following:

1. Member is 6 years of age or older; and
2. Recommended by a dermatologist; and

3. Member had inadequate response or inability to tolerate ONE of the following: topical calcipotriene containing products, topical anthralin, topical steroids, topical immune modulators (Elidel®, Protopic), topical retinoids; and
4. One of the following:
    a. BOTH of the following:
        i. Inadequate response or inability to tolerate THREE of the following: certolizumab (Cimzia®), adalimumab (Humira®), ustekinumab (Stelara®), guselkumab (Tremfya®) or risankizumab (Skyrizi™); and
        ii. Inadequate response or inability to tolerate ixekizumab (Taltz®); or
    b. Continuation of therapy with the requested product; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA: Ixekizumab (Taltz™) is approved when there is diagnosis of moderate to severe chronic plaque psoriasis and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a dermatologist; and
3. Member had inadequate response or inability to tolerate ONE of the following: topical calcipotriene containing products, topical anthralin, topical steroids, topical immune modulators (Elidel®, Protopic), topical retinoids; and
4. One of the following:
    a. Inadequate response or inability to tolerate ONE of the following: adalimumab (Humira®), ustekinumab (Stelara®), certolizumab (Cimzia®), risankizumab (Skyrizi™) or guselkumab (Tremfya®); or
    b. Continuation of therapy with the requested product; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA Etanercept (Enbrel®) is approved when there is diagnosis of moderate to severe chronic plaque psoriasis and ALL of the following:

1. Member is 4 years of age or older; and
2. Recommended by a dermatologist; and
3. Member had inadequate response or inability to tolerate ONE of the following: topical calcipotriene containing products, topical anthralin, topical steroids, topical immune modulators (Elidel®, Protopic), topical retinoids; and
4. One of the following:
    a. BOTH of the following:
        i. Inadequate response or inability to tolerate THREE of the following: certolizumab (Cimzia®), adalimumab (Humira®), ustekinumab (Stelara®), guselkumab (Tremfya®) or risankizumab (Skyrizi™); and
        ii. Inadequate response or inability to tolerate ixekizumab (Taltz®); or
    b. Continuation of therapy with the requested product; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonist)

INITIAL CRITERIA: Methotrexate injection (i.e., Otrexup™, Rasuvo®, Reditrex™) is approved when there is a diagnosis of severe psoriasis and ALL of the following:

1. Member is age 18 years or older
2. Recommended by a dermatologist
3. Inadequate response to ALL other standard therapy (e.g., oral methotrexate, all topical therapy modalities, phototherapy, etc.); and
4. For Otrexup™ and Reditrex™ only: inadequate response or inability to tolerate Rasuvo®

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Adalimumab (Humira®), guselkumab (Tremfya®), certolizumab (Cimzia®), risankizumab (Skyrizi™), apremilast (Otezla®), ustekinumab (Stelara®), secukinumab (Cosentyx™), ixekizumab (Taltz™), etanercept (Enbrel®), or methotrexate injection (i.e., Otrexup™, Rasuvo®, Reditrex™) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

INITIAL CRITERIA Brodalumab (Siliq™) is approved when there is diagnosis of moderate to severe chronic plaque psoriasis and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a dermatologist; and
3. Member had inadequate response or inability to tolerate ONE of the following: topical calcipotriene containing products, topical anthralin, topical steroids, topical immune modulators (Elidel®, Protopic®), topical retinoids; and
4. One of the following:
    a. BOTH of the following:
        i. Inadequate response or inability to tolerate THREE of the following: adalimumab (Humira®), ustekinumab (Stelara®), certolizumab (Cimzia®), risankizumab (Skyrizi), or guselkumab (Tremfya®); and
        ii. Inadequate response or inability to tolerate ixekizumab (Taltz®); or

    b. Continuation of therapy with the requested product; and
5. Member has been evaluated for depression and suicidal ideations using the Patient Health Questionnaire (PHQ)-9; and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonist)

Initial authorization duration: 16 weeks

REAUTHORIZATION CRITERIA Brodalumab (Siliq™) is re-approved when there is documentation of BOTH of the following:

1. Member has positive response to therapy with brodalumab (Siliq®); and
2. Member has been evaluated for depression and suicidal ideations using the Patient Health Questionnaire (PHQ)-9

Reauthorization duration: 1 year

Crohn's Disease

INITIAL CRITERIA: Adalimumab (Humira®), certolizumab (Cimzia®), or ustekinumab (Stelara®) is approved when there is a diagnosis of moderate to severe Crohn's disease and ALL of the following:

1. Member is 6 years of age or older (adalimumab) or 18 years of age or older (certolizumab and ustekinumab); and
2. Recommended by a gastroenterologist; and
3. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
4. Member had inadequate response or inability to tolerate one drug from any of TWO of the following groups:
    a. Corticosteroids: budesonide (Entocort® EC), prednisone, hydrocortisone, methylprednisolone; or
    b. Aminosalicylates: sulfasalazine, mesalamine (Asacol®, Rowasa®, Canasa®, Pentasa®); or
    c. Immunomodulators: azathioprine, 6-mercaptopurine, cyclosporine, tacrolimus (Prograf®), methotrexate; or
    d. Antibiotics: metronidazole, levofloxacin

INITIAL CRITERIA: Methotrexate injection (i.e. Otrexup™, Rasuvo®, Reditrex™) is approved when there is a diagnosis of moderate to severe Crohn's disease and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a gastroenterologist; and
3. For Otrexup™ and Reditrex™ only: inadequate response or inability to tolerate Rasuvo®

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Adalimumab (Humira®), certolizumab (Cimzia®), ustekinumab (Stelara®), methotrexate injection (i.e., Otrexup™, Rasuvo®, Reditrex™) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Ulcerative Colitis (UC)

INITIAL CRITERIA: Ustekinumab (Stelara®), or golimumab (Simponi®) is approved when there is a diagnosis of moderate to severe UC and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a gastroenterologist; and
3. Member had inadequate response or inability to tolerate ONE of the following medications: corticosteroids, azathioprine, 6-mercaptopurine; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA: Adalimumab (Humira®) is approved when there is a diagnosis of moderate to severe UC and ALL of the following:

1. Member is 5 years of age or older; and
2. Recommended by a gastroenterologist; and
3. Member had inadequate response or inability to tolerate ONE of the following medications: corticosteroids, azathioprine, 6-mercaptopurine; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA: Tofacitinib (Xeljanz®/Xeljanz® XR tablets/extended-release tablets) is approved when there is diagnosis of moderate to severe UC and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a gastroenterologist; and
3. Member had inadequate response or inability to tolerate ONE of the following medications: corticosteroids, azathioprine, 6-mercaptopurine; and
4. One of the following:
    a. Member had inadequate response or inability to tolerate TWO of the following adalimumab (Humira®), ustekinumab (Stelara®), or golimumab (Simponi®); or
    b. Continuation of therapy with the requested product; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Adalimumab (Humira®), ustekinumab (Stelara®), or golimumab (Simponi®), or tofacitinib (Xeljanz® /Xeljanz® XR tablets/extended-release tablets) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Cryopyrin-Associated Periodic Syndromes (CAPS)

INITIAL CRITERIA: Anakinra (Kineret®) is approved when there is a diagnosis of Neonatal-Onset Multisystem Inflammatory Disease (NOMID) and BOTH of the following:

1. Recommended by a rheumatologist or other appropriate specialist; and
2. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA: Rilonacept (Arcalyst®) is approved when there is a diagnosis of Cryopyrin-Associated Periodic Syndromes including Familial cold Auto-Inflammatory Syndrome (FCAS) and/or Muckle-Wells Syndrome (MWS) and ALL of the following :

1. Prescribed by or in consultation with an immunologist, allergist, dermatologist, rheumatologist, neurologist, or other medical specialist; and
2. Member is 12 years of age or older; and
3. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Anakinra (Kineret®) or rilonacept (Arcalyst®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Hidradenitis Suppurativa

INITIAL CRITERIA: Adalimumab (Humira®) is approved when there is a diagnosis of moderate to severe hidradenitis suppurativa (i.e. Hurley stage II or III) and BOTH of the following:

1. Recommended by a dermatologist; and
2. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
3. Member is 12 years of age or older

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Adalimumab (Humira®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Uveitis

INITIAL CRITERIA: Adalimumab (Humira®) is approved when there is a diagnosis of non-infectious intermediate, posterior, or panuveitis and ALL of the following:

1. Recommended by an ophthalmologist; and
2. Member had inadequate response or inability to tolerate ophthalmic and oral corticosteroids; and
3. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
4. Member is 2 years of age or older

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Adalimumab (Humira®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Giant Cell Arteritis

INITIAL CRITERIA: Tocilizumab (Actemra® SQ) is approved when there is a diagnosis of Giant cell arteritis and ALL of the following:

1. Recommended by a rheumatologist; and
2. Member is 18 years of age or older; and
3. Member had inadequate response or inability to tolerate a glucocorticoid (i.e. prednisone); and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Tocilizumab (Actemra® SQ) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Systemic Juvenile Idiopathic Arthritis

INITIAL CRITERIA: Tocilizumab (Actemra® SQ) is approved when there is diagnosis of active systemic juvenile idiopathic arthritis (SIJA) and ALL of the following:

1. Recommended by a rheumatologist; and
2. Member is 2 years of age or older; and
3. Inadequate response or inability to tolerate ONE of the following:
    a. Non-steroidal anti-inflammatory drug (NSAID) (e.g., ibuprofen); or
    b. Systemic glucocorticoid (e.g., prednisone)
    c. DMARDs (e.g., leflunomide, methotrexate)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Tocilizumab (Actemra® SQ) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Non-radiographic axial spondyloarthritis (nr-axSpA)

INITIAL CRITERIA: Certolizumab (Cimzia®) is approved when there is a diagnosis of active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a rheumatologist; and
3. No concurrent therapy with any other biologic DMARD (i.e. tumor necrosis factor antagonists)

INITIAL CRITERIA: Ixekizumab (Taltz®) is approved when there is a diagnosis of active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a rheumatologist; and
3. One of the following:
    a. Inadequate response or inability to tolerate certolizumab (Cimzia®); or
    b. Continuation of therapy with the requested product; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

INITIAL CRITERIA: Secukinumab (Cosentyx®) is approved when there is a diagnosis of active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation and ALL of the following:

1. Member is 18 years of age or older; and
2. Recommended by a rheumatologist; and
3. One of the following:
    a. Inadequate response or inability to tolerate BOTH of the following: certolizumab (Cimzia®) and Ixekizumab (Taltz®); or
    b. Continuation of therapy with the requested product; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Tocilizumab Certolizumab (Cimzia®), ixekizumab (Taltz®), or secukinumab (Cosentyx®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Ulcer of the mouth associated with Behcet's syndrome

INITIAL CRITERIA: Apremilast (Otezla®) is approved when there is a diagnosis of ulcer of the mouth associated with Behcet's syndrome and ALL of the following:

1. Member is 18 years of age or older; and
2. Prescribed by or in consultation with a rheumatologist or dermatologist; and
3. Inadequate response or inability to tolerate systemic corticosteroids, topical corticosteroids or topical sucralfate; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Apremilast (Otezla®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Deficiency of Interleukin-1 Receptor Antagonist (DIRA)

INITIAL CRITERIA: Rilonacept (Arcalyst®) is approved when used for the maintenance of remission of Deficiency of Interleukin-1 Receptor Antagonist (DIRA) and ALL of the following:

1. Member weights at least 10kg; and

2. Prescribed by or in consultation with a rheumatologist or pediatric specialist; and
3. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonist)

INITIAL CRITERIA: Anakinra (Kineret®) is approved when there is diagnosis of Deficiency of Interleukin-1 Receptor Antagonist (DIRA) and BOTH of the following:
1. Prescribed by or in consultation with a rheumatologist or pediatric specialist; and
2. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonist)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Rilonacept (Arcalyst®) or anakinra (Kineret®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Recurrent pericarditis

INITIAL CRITERIA: Rilonacept (Arcalyst®) is approved when used for the treatment of recurrent pericarditis and reduction in risk of recurrence and ALL of the following:
1. Member is 12 years of age or older; and
2. Prescribed by or in consultation with a cardiologist; and
3. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Rilonacept (Arcalyst®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Systemic sclerosis-associated interstitial lung disease (SSc-ILD)

INITIAL CRITERIA: Tocilizumab (Actemra®) is approved when used for diagnosis of SSc-ILD confirmed by a High-Resolution CT scan or biopsy and ALL of the following:
1. Member is 18 years of age or older; and
2. Inadequate response or inability to tolerate one of the following:
    a. Mycophenolate; or
    b. Cyclophosphamide; or
    c. Azathioprine; and
3. Prescribed by or in consultation with a pulmonologist; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Tocilizumab (Actemra®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Black Box Warning as shown in the drug Prescribing Information:

Adalimumab (Humira®)
SERIOUS INFECTIONS

- Patients treated with HUMIRA are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.
- Discontinue HUMIRA if a patient develops a serious infection or sepsis.
- Reported infections include:
    - Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Test patients for latent TB before HUMIRA use and during therapy. Initiate treatment for latent TB prior to HUMIRA use.

- Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Consider empiric anti-fungal therapy in patients at risk for invasive fungal infections who develop severe systemic illness.

- Bacterial, viral and other infections due to opportunistic pathogens, including Legionella and Listeria.

- Carefully consider the risks and benefits of treatment with HUMIRA prior to initiating therapy in patients with chronic or recurrent infection.

- Monitor patients closely for the development of signs and symptoms of infection during and after treatment with HUMIRA, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.

MALIGNANCY

- Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers including HUMIRA. Post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including HUMIRA. These cases have had a very aggressive disease course and have been fatal. The majority of reported TNF blocker cases have occurred in patients with Crohn's disease or ulcerative colitis and the majority were in adolescent and young adult males. Almost all these patients had received treatment with azathioprine or 6-mercaptopurine (6–MP) concomitantly with a TNF blocker at or prior to diagnosis. It is uncertain whether the occurrence of HSTCL is related to use of a TNF blocker or a TNF blocker in combination with these other immunosuppressants.

Baricitinib (Olumiant®)

SERIOUS INFECTIONS

- Patients treated with OLUMIANT are at risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.
- If a serious infection develops, interrupt OLUMIANT until the infection is controlled.
  Reported infections include:
  - Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before initiating OLUMIANT and during therapy. Treatment for latent infection should be considered prior to OLUMIANT use.
  - Invasive fungal infections, including candidiasis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.
  - Bacterial, viral, and other infections due to opportunistic pathogens.
- The risks and benefits of treatment with OLUMIANT should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.
- Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with OLUMIANT including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

MALIGNANCIES

Lymphoma and other malignancies have been observed in patients treated with OLUMIANT.

THROMBOSIS

Thrombosis, including deep venous thrombosis and pulmonary embolism, has been observed at an increased incidence in patients treated with OLUMIANT compared to placebo. In addition, there were cases of arterial thrombosis. Many of these adverse events were serious and some resulted in death. Patients with symptoms of thrombosis should be promptly evaluated.

Brodalumab (Siliq™)

SUICIDAL IDEATION AND BEHAVIOR

Suicidal ideation and behavior, including completed suicides, have occurred in patients treated with SILIQ. Prior to prescribing SILIQ, weigh the potential risks and benefits in patients with a history of depression and/or suicidal ideation or behavior. Patients with new or worsening suicidal ideation and behavior should be referred to a mental health professional, as appropriate. Advise patients and caregivers to seek medical attention for manifestations of suicidal ideation or behavior, new onset or worsening depression, anxiety, or other mood changes

Because of the observed suicidal behavior in subjects treated with SILIQ, SILIQ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the SILIQ REMS Program.

Certolizumab (Cimzia®)

SERIOUS INFECTIONS

- Patients treated with CIMZIA are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.
- CIMZIA should be discontinued if a patient develops a serious infection or sepsis.
- Reported infections include:
    - Active tuberculosis, including reactivation of latent tuberculosis. Patients with tuberculosis have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent tuberculosis before CIMZIA use and during therapy. Treatment for latent infection should be initiated prior to CIMZIA use.
    - Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Empiric anti-fungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.
    - Bacterial, viral and other infections due to opportunistic pathogens, including Legionella and Listeria.
- The risks and benefits of treatment with CIMZIA should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.
- Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with CIMZIA, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

MALIGNANCY

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which CIMZIA is a member. CIMZIA is not indicated for use in pediatric patients.

Etanercept (Enbrel®)

SERIOUS INFECTIONS

- Patients treated with Enbrel are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.
- Enbrel should be discontinued if a patient develops a serious infection or sepsis.
- Reported infections include:
    - Active tuberculosis, including reactivation of latent tuberculosis. Patients with tuberculosis have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent tuberculosis before Enbrel use and during therapy. Treatment for latent infection should be initiated prior to Enbrel use.
    - Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Empiric anti-fungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.
    - Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella and Listeria.
- The risks and benefits of treatment with Enbrel should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.
- Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with Enbrel, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

MALIGNANCIES

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, including Enbrel.

Golimumab (Simponi®)

SERIOUS INFECTIONS

- Patients treated with SIMPONI® are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.
- Discontinue SIMPONI if a patient develops a serious infection.
- Reported infections with TNF blockers, of which SIMPONI is a member, include:
    - Active tuberculosis, including reactivation of latent tuberculosis. Patients with tuberculosis have frequently presented with disseminated or extrapulmonary disease. Test patients for latent tuberculosis before SIMPONI use and during therapy. Initiate treatment for latent TB prior to SIMPONI use.
    - Invasive fungal infections including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Consider empiric antifungal therapy in patients at risk for invasive fungal infections who develop severe systemic illness.
    - Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella and Listeria.
- Consider the risks and benefits of treatment with SIMPONI prior to initiating therapy in patients with chronic or recurrent infection.
- Monitor patients closely for the development of signs and symptoms of infection during and after treatment with SIMPONI, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

MALIGNANCY

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which SIMPONI is a member.

Sarilumab (Kevzara®)

- Patients treated with Kevzara® are at increased risk for developing serious infections that may lead to hospitalization or death. Opportunistic infections have also been reported in patients receiving Kevzara®. Most patients who developed infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.
- Avoid use of Kevzara® in patients with an active infection.
- Reported infections include:
    - Active tuberculosis, which may resent with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before Kevzara® use and during therapy. Treatment for latent infection should be initiated prior to Kevzara® use.
    - Invasive fungal infections, such as candidiasis, and pneumocystis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.
    - Bacterial, viral and other infections due to opportunistic pathogens.
- Closely monitor patients for signs and symptoms of infection during treatment with Kevzara®. If a serious infection develops, interrupt Kevzara® until the infection is controlled.
- Consider the risks and benefits of treatment with Kevzara® prior to initiating therapy in patients with chronic or recurrent infection.

Tocilizumab (Actemra® SQ)

- Patients treated with ACTEMRA are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.
- If a serious infection develops, interrupt ACTEMRA until the infection is controlled.
- Reported infections include:
    - Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before ACTEMRA use and during therapy. Treatment for latent infection should be initiated prior to ACTEMRA use.
    - Invasive fungal infections, including candidiasis, aspergillosis, and pneumocystis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.
    - Bacterial, viral and other infections due to opportunistic pathogens.
- The risks and benefits of treatment with ACTEMRA should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.
- Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with ACTEMRA, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

Tofacitinib (Xeljanz [XR]®)

SERIOUS INFECTIONS

- Patients treated with XELJANZ/XELJANZ XR/XELJANZ Oral Solution are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.
- If a serious infection develops, interrupt XELJANZ/XELJANZ XR/XELJANZ Oral Solution until the infection is controlled.
- Reported infections include:
    - Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before XELJANZ/XELJANZ XR/XELJANZ Oral Solution use and during therapy. Treatment for latent infection should be initiated prior to XELJANZ/XELJANZ XR/XELJANZ Oral Solution use.
    - Invasive fungal infections, including cryptococcosis and pneumocystosis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.
    - Bacterial, viral, including herpes zoster, and other infections due to opportunistic pathogens.
- The risks and benefits of treatment with XELJANZ/XELJANZ XR/XELJANZ Oral Solution should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.
- Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with XELJANZ/XELJANZ XR/XELJANZ Oral Solution, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

MORTALITY

Rheumatoid arthritis patients 50 years of age and older with at least one cardiovascular (CV) risk factor treated with XELJANZ 10 mg twice a day had a higher rate of all-cause mortality, including sudden CV death, compared to those treated with XELJANZ 5 mg given twice daily or TNF blockers in a large, ongoing, postmarketing safety study.

MALIGNANCIES

Lymphoma and other malignancies have been observed in patients treated with XELJANZ. Epstein Barr Virus-associated post-transplant lymphoproliferative disorder has been observed at an increased rate in renal transplant patients treated with XELJANZ and concomitant immunosuppressive medications.

THROMBOSIS

Thrombosis, including pulmonary embolism, deep venous thrombosis, and arterial thrombosis, has been observed at an increased incidence in rheumatoid arthritis patients who were 50 years of age and older with at least one CV risk factor treated with XELJANZ 10 mg twice daily compared to XELJANZ 5 mg twice daily or TNF blockers in a large, ongoing postmarketing safety study. Many of these events were serious and some resulted in death. Avoid XELJANZ/XELJANZ XR in patients at risk. Discontinue XELJANZ/XELJANZ XR and promptly evaluate patients with symptoms of thrombosis.

For patients with ulcerative colitis, use XELJANZ at the lowest effective dose and for the shortest duration needed to achieve/maintain therapeutic response.

Methotrexate (Otrexup™, Rasuvo®, Reditrex™)

- Serious toxic reactions and death have been reported with the use of methotrexate. Patients should be closely monitored for bone marrow, liver, lung, skin, and kidney toxicities.
- Methotrexate has been reported to cause fetal death and/or congenital anomalies and is contraindicated in pregnancy.
- Unexpectedly severe (sometimes fatal) bone marrow suppression, aplastic anemia, and gastrointestinal toxicity have been reported with concomitant administration of methotrexate (usually in high dosage) along with some nonsteroidal anti-inflammatory drugs (NSAIDs).
- Hepatotoxicity, fibrosis, and cirrhosis may occur after prolonged use.
- Methotrexate may cause interstitial pneumonitis at any time during therapy and has been reported at low doses. Pulmonary symptoms (especially a dry, nonproductive cough) may require interruption of treatment and careful investigation.
- Diarrhea, ulcerative stomatitis, hemorrhagic enteritis, and death from intestinal perforation may occur.
- Severe, occasionally fatal, skin reactions have been reported.
- Potentially fatal opportunistic infections may occur.

Upadacitinib (Rinvoq™)

SERIOUS INFECTIONS

- Patients treated with RINVOQ are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.
- If a serious infection develops, interrupt RINVOQ until the infection is controlled.

- Reported infections include:
    - Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before RINVOQ use and during therapy. Treatment for latent infection should be considered prior to RINVOQ use.
    - Invasive fungal infections, including cryptococcosis and pneumocystosis.
    - Bacterial, viral, including herpes zoster, and other infections due to opportunistic pathogens.
- The risks and benefits of treatment with RINVOQ should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.
- Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with RINVOQ, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

MALIGNANCIES

Lymphoma and other malignancies have been observed in patients treated with RINVOQ

THROMBOSIS

Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis have occurred in patients treated with Janus kinase inhibitors used to treat inflammatory conditions. Many of these adverse events were serious and some resulted in death. Consider the risks and benefits prior to treating patients who may be at increased risk. Patients with symptoms of thrombosis should be promptly evaluated and treated appropriately.

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

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Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Actemra® SQ	tocilizumab
Cimzia®	certolizumab
Cosentyx™	secukinumab
Enbrel®	etanercept
Humira®	adalimumab
Kineret®	anakinra
Simponi®	golimumab
Orencia®	abatacept
Otezla®	apremilast
Xeljanz [XR]®	tofacitinib
Otrexup®, Rasuvo™, Reditrex™	methotrexate
Taltz™	ixekizumab
Kevzara®	sarilumab
Siliq™	brodalumab
Stelara®	ustekinumab
Tremfya®	guselkumab
Olumiant®	baricitinib
Arcalyst®	rilonacept
Skyrizi™	risankizumab-rzaa
Rinovq™	upadacitinib

Cross References:

Off-Label Use Rx.01.33

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