

Pharmacy Policy Bulletin

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®)**, **ustekinumab (Stelara®)**, **izekizumab (Taltz®)**, **sarilumab (Kevzara®)**, **brodalumab (Siliq™)**, **rilonacept (Arcalyst®)**, **baricitinib (Olumiant®)** and **guselkumab (Tremfya®)** 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 × 10⁻¹⁰M).

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

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 antagonist 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.

Methotrexate injection (Otrexup™, Rasuvo®) 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.

Summary Tables

Table 1: Non-biologics

INDICATION/ AGENT	AS	CD	NOMID/CAPS	PP	Polyarticular JIA	PA	RA	Systemic JIA	UC
Otelza® (apremilast)				X		X			
Otrexup®, Rasuvo® (methotrexate)				X	X		X		

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

INDICATION/ AGENT	AS	CD	NOMID	PP	Polyarticular JIA	PA	RA	Systemic JIA	UC	GCA	CAPS/ FCAS/MWS
Actemra® (tocilizumab)					X		X	X		X	
Stelara® (ustekinumab)		X		X		X					
Cosentyx® (secukinumab)	X			X		X					
Taltz® (izekizumab)				X		X					
Kineret® (anakinra)			X				X				
Orencia® SQ (abatacept)					X	X	X				
Xeljanz® [XR] (tofacitinib)						X	X				
Kevzara® (sarilumab)							X				
Siliq™ (brodalumab)				X							
Tremfya® (guselkumab)				X							
Olumiant® (baricitinib)							X				
Arcalyst® (rilonacept)											X

Table 3: Anti-TNF Biologics

INDICATION/ AGENT	AS	CD	HS	NOMID/CAPS	PP	Polyarticular JIA	PA	RA	Systemic JIA	UC	Uveitis
Cimzia® (certolizumab)	X	X						X	X		

Enbrel (etanercept)	X				X (starting at age 4)	X	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
Polyarticular JIA	Polyarticular Juvenile Idiopathic Arthritis
PA	Psoriatic Arthritis
RA	Rheumatoid Arthritis
Systemic JIA	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)

Policy:

A. Rheumatoid Arthritis (RA)

1. Adalimumab (Humira®) or certolizumab (Cimzia®) is approved when there is a diagnosis of moderate to severe RA and ALL of the following:
 - a. Member is 18 years of age or older; and
 - b. Recommended by a rheumatologist; and
 - c. Member had inadequate response or inability to tolerate ONE of the following disease-modifying anti-rheumatic drugs (DMARDs): methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
 - d. No concurrent therapy with any other biologic DMARD (ie tumor necrosis factor antagonists)
2. Golimumab (Simponi®) is approved when there is a diagnosis of moderate to severe RA and ALL of the following:
 - a. Member is 18 years of age or older; and
 - b. Recommended by a rheumatologist; and
 - c. Used in conjunction with methotrexate; and
 - d. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)
3. Abatacept (Orencia® SQ), anakinra (Kineret®), etanercept (Enbrel®), sarilumab (Kevzara®), baricitinib (Olumiant®) or tocilizumab (Actemra® SQ) is approved when there is a diagnosis of moderate to severe RA and ALL of the following:
 - a. Member is 18 years of age or older; and
 - b. Recommended by a rheumatologist; and
 - c. Inadequate response or inability to tolerate TWO of the following: adalimumab (Humira®), certolizumab (Cimzia®), or golimumab (Simponi®) or documentation demonstrating a trial may be inappropriate; and
 - d. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)
4. Tofacitinib (Xeljanz®) is approved when there is a diagnosis of moderate to severe RA and ALL of the following:
 - a. Member is 18 years of age or older; and
 - b. Recommended by a rheumatologist; and
 - c. Inadequate response or inability to tolerate methotrexate; and
 - d. Inadequate response or inability to tolerate TWO of the following: adalimumab (Humira®), certolizumab (Cimzia®), or golimumab (Simponi®) or documentation demonstrating a trial may be inappropriate; and
 - e. No concurrent therapy with either of the following:
 - i. A biologic DMARD (i.e., tumor necrosis factor antagonists); or
 - ii. A potent immunosuppressant (i.e., azathioprine, cyclosporine)
5. Methotrexate injection (Otrexup™, Rasuvo®) is approved when there is diagnosis of severe, active rheumatoid arthritis (RA) and ALL of the following:
 - a. Recommended by a rheumatologist; and
 - b. Inadequate response or inability to tolerate oral methotrexate

B. Ankylosing Spondylitis (AS)

1. Adalimumab (Humira®), certolizumab (Cimzia®), or golimumab (Simponi®) is approved when there is a diagnosis of AS and ALL of the following:
 - a. Member is 18 years of age or older; and
 - b. Recommended by a rheumatologist; and

- c. Member had inadequate response or inability to tolerate ONE of the following disease-modifying anti-rheumatic drugs (DMARDs): methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
 - d. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)
2. Etanercept (Enbrel®) or secukinumab (Cosentyx®) is approved when there is a diagnosis of active AS and ALL of the following:
 - a. Member is 18 years of age or older; and
 - b. Recommended by a rheumatologist; and
 - c. Inadequate response or inability to tolerate TWO of the following: adalimumab (Humira®), certolizumab (Cimzia®), or golimumab (Simponi®) or documentation demonstrating a trial may be inappropriate; and
 - d. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

C. Polyarticular Juvenile Idiopathic Arthritic (PJIA)

1. Adalimumab (Humira®) is approved when there is a diagnosis of moderate to severe PJIA and ALL of the following:
 - a. Member is 2 years of age or older; and
 - b. Recommended by a rheumatologist; and
 - c. Inadequate response or inability to tolerate ONE of the following DMARDs: methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
 - d. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)
2. Etanercept (Enbrel®), tocilizumab (Actemra® SQ), abatacept (Orencia® SQ) is approved when there is a diagnosis of moderate to severe PJIA and ALL of the following:
 - a. Member is 2 years of age or older; and
 - b. Recommended by a rheumatologist; and
 - c. Inadequate response or inability to tolerate adalimumab (Humira®) or documentation demonstrating a trial may be inappropriate; and
 - d. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)
3. Methotrexate injection (Otrexup™, Rasuvo®) is approved when there is diagnosis of polyarticular juvenile idiopathic arthritis (pJIA) and ALL of the following:
 - a. recommended by a rheumatologist; and
 - b. inadequate response or inability to tolerate oral methotrexate

D. Psoriatic Arthritis

1. Adalimumab (Humira®), certolizumab (Cimzia®), ustekinumab (Stelara®), apremilast (Otezla®), or golimumab (Simponi®) is approved when there is a diagnosis of moderate to severe psoriatic arthritis and ALL of the following:
 - a. Member is 18 years of age or older; and
 - b. Recommended by a rheumatologist; and
 - c. Member had inadequate response or inability to tolerate ONE of the following disease-modifying anti-rheumatic drugs (DMARDs): methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
 - d. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)
2. Etanercept (Enbrel®), abatacept (Orencia®), or secukinumab (Cosentyx), ixekizumab (Taltz®) or tofacitinib (Xeljanz®/Xeljanz® XR) is approved when there is a diagnosis of moderate to severe psoriatic arthritis and ALL of the following:
 - a. Member is 18 years of age or older; and

- b. Recommended by a rheumatologist or dermatologist; and
 - c. Inadequate response or inability to tolerate TWO of the following: adalimumab (Humira®), certolizumab (Cimzia®), golimumab (Simponi®), or ustekinumab (Stelara®), or documentation demonstrating a trial may be inappropriate; and
 - d. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)
3. Methotrexate injection (Otrexup®, Rasuvo®) is approved when there is diagnosis of psoriatic arthritis (PsA) and ALL of the following:
- a. Recommended by a rheumatologist; and
 - b. Inadequate response or inability to tolerate oral methotrexate

E. Plaque Psoriasis

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

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

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

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

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

- a. Member is 18 years of age or older; and
- b. Recommended by a dermatologist; and
- c. 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
- d. Inadequate response or inability to tolerate ONE of the following or documentation demonstrating a trial may be inappropriate:
 - i. Adalimumab (Humira®)
 - ii. Ustekinumab (Stelara®)
 - iii. Guselkumab (Tremfya®)
 - iv. Certolizumab (Cimzia®)

4. Izekizumab (Taltz™) is approved when there is diagnosis of moderate to severe chronic plaque psoriasis and ALL of the following:

- a. Member is 18 years of age or older; and
- b. Recommended by a dermatologist; and
- c. 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
- d. Inadequate response or inability to tolerate TWO of the following: adalimumab (Humira®), ustekinumab (Stelara®), certolizumab (Cimzia®) or guselkumab (Tremfya®) or documentation demonstrating a trial may be inappropriate

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

- i. Member is 4 years of age or older; and
- ii. Recommended by a dermatologist; and
- iii. 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
- iv. Inadequate response or inability to tolerate adalimumab (Humira®), ustekinumab (Stelara®), certolizumab (Cimzia®), guselkumab (Tremfya®) or documentation demonstrating a trial may be inappropriate

6. Methotrexate injection (Otrexup™, Rasuvo®) is approved when any of the following inclusion criteria is met:

- a. Diagnosis of severe psoriasis and ALL of the following:
 - i. Member is age 18 years or older
 - ii. Recommended by a dermatologist
 - iii. Inadequate response to ALL other standard therapy (e.g., oral methotrexate, all topical therapy modalities, phototherapy, etc.)

7. Initial Criteria: Brodalumab (Siliq™) is approved when there is diagnosis of moderate to severe chronic plaque psoriasis and ALL of the following:

- a. Member is 18 years of age or older; and
- b. Recommended by a dermatologist; and
- c. 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
- d. Inadequate response or inability to tolerate adalimumab (Humira®) ustekinumab (Stelara®), certolizumab (Cimzia®), or guselkumab (Tremfya®) or documentation demonstrating a trial may be inappropriate; and
- e. Member has been evaluated for depression and suicidal ideations using the Patient Health Questionnaire (PHQ)-9

Initial authorization duration: 16 weeks

Reauthorization criteria:

Brodalumab (Siliq™) is reapproved when there is documentation of BOTH of the following:

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

Reauthorization duration: 1 year

F. Crohn's Disease

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

G. Ulcerative Colitis (UC)

1. Adalimumab (Humira®) or golimumab (Simponi®) is approved when there is a diagnosis of moderate to severe UC and ALL of the following:
 - a. Member is 18 years of age or older; and
 - b. Recommended by a gastroenterologist; and
 - c. Patient had inadequate response or inability to tolerate ONE of the following medications: corticosteroids, azathioprine, 6-mercaptopurine; and
 - d. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)
2. Tofacitinib (Xeljanz®) is approved when there is diagnosis of moderate to severe UC and ALL of the following:
 - a. Member is 18 years of age or older; and
 - b. Recommended by a gastroenterologist; and
 - c. Patient had inadequate response or inability to tolerate ONE of the following medications: corticosteroids, azathioprine, 6-mercaptopurine; and
 - d. Patient had inadequate response or inability to tolerate Humira® and Simponi®

- e. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

H. Cryopyrin-Associated Periodic Syndromes (CAPS)

1. Anakinra (Kineret®) is approved when there is a diagnosis of NOMID and BOTH of the following:
 - a. Recommended by a rheumatologist or other appropriate specialist; and
 - b. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)
2. 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 :
 - a. Prescribed by or in consultation with an immunologist, allergist, dermatologist, rheumatologist, neurologist, or other medical specialist; and
 - b. Member is 12 years of age or older; and
 - c. No concurrent therapy with any other biologic DMARD (i.e. tumor necrosis factor antagonists)

I. Hidradenitis Suppurativa

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

J. Uveitis

1. Adalimumab (Humira®) is approved when there is a diagnosis of non-infectious intermediate, posterior, or panuveitis and ALL of the following:
 - a. Recommended by an ophthalmologist; and
 - b. Member had inadequate response or inability to tolerate ophthalmic and oral corticosteroids; and
 - c. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
 - d. Member is 2 years of age or older

K. Giant Cell Arteritis

1. Tocilizumab (Actemra® SQ) is approved when there is a diagnosis of Giant cell arteritis and ALL of the following:
 - a. Recommended by a rheumatologist; and
 - b. Member is 18 years of age or older; and
 - c. Member had inadequate response or inability to tolerate a glucocorticoid (i.e. prednisone); and
 - d. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists)

L. Systemic Juvenile Idiopathic Arthritis

1. Tocilizumab (Actemra® SQ) is approved when there is diagnosis of active systemic juvenile idiopathic arthritis (SIJA) and BOTH of the following:
 - a. Recommended by a rheumatologist;
 - b. Member is 2 years of age or older

Black Box Warning:

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 immunosuppressant.

Baricitinib (Olumiant®)

SERIOUS INFECTIONS

Patients treated with OLUMIANT are at risk for developing serious infections that may lead to hospitalization or death [see Warnings and Precautions (5.1) and Adverse Reactions (6.1)]. 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 [see Warnings and Precautions (5.1)].

MALIGNANCIES

Lymphoma and other malignancies have been observed in patients treated with OLUMIANT [see Warnings and Precautions (5.2)].

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. [See Warnings and Precautions (5.3)].

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

- Increased risk of serious infections leading to hospitalization or death, including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens.
- Enbrel should be discontinued if a patient develops a serious infection or sepsis during treatment.
- Perform test for latent TB; if positive, start treatment for TB prior to starting Enbrel.
- Monitor all patients for active TB during treatment, even if initial latent TB test is negative.

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 leading to hospitalization or death including tuberculosis (TB), bacterial sepsis, invasive fungal (such as histoplasmosis), and other opportunistic infections have occurred in patients receiving SIMPONI
- Discontinue SIMPONI if a patient develops a serious infection or sepsis
- Perform test for latent TB; if positive, start treatment for TB prior to starting SIMPONI
- Monitor all patients for active TB during treatment, even if initial latent TB test is negative
- Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, 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 present 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)

- Serious infections leading to hospitalization or death including tuberculosis (TB), bacterial, invasive fungal, viral, and other opportunistic infections have occurred in patients receiving ACTEMRA.
- If a serious infection develops, interrupt ACTEMRA until the infection is controlled.
- Perform test for latent TB; if positive, start treatment for TB prior to starting ACTEMRA.
- Monitor all patients for active TB during treatment, even if initial latent TB test is negative.

Tofacitinib (Xeljanz [XR]®)

- Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving XELJANZ.
- If a serious infection develops, interrupt XELJANZ until the infection is controlled.
- Prior to starting XELJANZ, perform a test for latent tuberculosis; if it is positive, start treatment for tuberculosis prior to starting XELJANZ.
- Monitor all patients for active tuberculosis during treatment, even if the initial latent tuberculosis test is negative.
- 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.

Methotrexate (Otrexup™, Rasuvo®)

- 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.

▸ 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™	methotrexate
Taltz™	izekizumab
Kevzara®	sarilumab
Siliq™	brodalumab
Stelara®	ustekinumab
Tremfya®	guselkumab
Olumiant®	baricitinib
Arcalyst®	rilonacept

Cross References:

N/A

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The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.