Medical Policy

BlueCross BlueShield of Kansas
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Title: Biologic Immunomodulators Therapy (Pharmacy Benefit Only)

- **Prime Therapeutics will review Prior Authorization requests.**
  Prior Authorization Form:
  https://www.bcbsks.com/CustomerService/Forms/pdf/PriorAuth-6292KS-BIOL.pdf

  Link to Drug List (Formulary):
  https://www.bcbsks.com/drugs/

Professional
Original Effective Date: June 1, 2011
Revision Date(s): July 19, 2011; November 1, 2011; November 19, 2012; December 27, 2012; March 1, 2013; June 7, 2013; December 2, 2013; January 1, 2014; June 1, 2014; August 15, 2014; October 1, 2014; May 1, 2015; July 1, 2015; September 1, 2015; January 1, 2016; May 1, 2016, July 1, 2016; July 25, 2016; September 1, 2016; October 1, 2016; December 1, 2016; January 1, 2017, July 1, 2017; October 1, 2017; October 15, 2017; January 1, 2018; January 26, 2018, May 21, 2018; June 15, 2018; June 18, 2018; July 2, 2018; July 16, 2018; August 20, 2018; September 1, 2018
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Institutional
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Current Effective Date: September 1, 2018

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

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The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

DESCRIPTION

The intent of the Biologic Immunomodulators Prior Authorization with Quantity Limit criteria is to ensure appropriate therapy according to Food and Drug Administration (FDA)-approved product labeling and/or clinical guidelines and/or clinical trials. The targeted agents are self-administered biologic immunomodulator agents. The criteria will encourage the use of first-line conventional agents, some of which are available as generics (for example, first-line agents for arthritis, are methotrexate and leflunomide, which are both available as generics). If a plan has preferred agents criteria will also encourage use of two preferred biologic immunomodulators when clinically appropriate before the nonpreferred agents with appropriate dosing. This program allows continuation of therapy when patients have been receiving and are stabilized on the requested agent.

Target Agents

Preferred and Nonpreferred Biologic Immunomodulators		
Preferred Agents	**Non-preferred Agents**	
Cosentyx Enbrel Humira Simponi Stelara	Actemra Cimzia Kevzara Kineret Olumiant Orencia	Taltz Tremfya Siliq Xeljanz Xeljanz XR

Disease State	Try/Fail	Preferred	Non-preferred
Rheumatoid Disorders			
Ankylosing Spondylitis (AS)	Try/Fail 3 preferred agents	SQ: Cosentyx, Enbrel, Humira, Simponi	SQ: Cimzia
Polyarticular Juvenile Idiopathic Arthritis (PJIA)	Try/Fail 2 preferred agents	SQ: Enbrel, Humira	SQ: Actemra, Orencia
Psoriatic Arthritis (PsA)	Try/Fail 3 preferred agents	SQ: Cosentyx, Enbrel, Humira, Simponi, Stelara	Oral: Xeljanz, Xeljanz XR SQ: Cimzia, Orencia, Taltz
Rheumatoid Arthritis	Try/Fail 2 preferred agents; then must try Xeljanz or Xeljanz XR prior to any other non-preferred agent (last preferred agent is still approvable prior to Xeljanz (XR))	SQ: Enbrel, Humira, Simponi	Oral: Olumiant, Xeljanz, Xeljanz XR SQ: Cimzia, Kevzara, Kineret, Orencia
Dermatological Disorder			
Hidradenitis Suppurativa (HS)	Try/Fail 1 preferred agent	SQ: Humira	N/A
Psoriasis (PS)	Try/Fail 3 preferred agents	SQ: Cosentyx, Enbrel, Humira, Stelara	SQ: Cimzia, Siliq, Taltz, Tremfya

Disease State	Try/Fail	Preferred	Non-preferred
Inflammatory Bowel Disease			
Crohn's Disease	Try/Fail 2 preferred agents	SQ: Humira, Stelara	SQ: Cimzia
Ulcerative Colitis	Try/Fail 2 preferred agents	SQ: Humira, Simponi	Oral: Xeljanz
Other			
Uveitis	Try/Fail 1 preferred agent	SQ: Humira	N/A
Indications Without Preferred Agents Required			
Cytokine Release Syndrome (CRS), Neonatal-Onset Multisystem Inflammatory Disease (NOMID), Systemic Juvenile Idiopathic Arthritis (SJIA)	N/A	N/A	N/A

*For patients with preferred Remicade (infliximab) and infliximab biosimilars, Remicade is preferred agent prior to use of Inflectra and Renflexis

FDA Approved Indications and Dosage[1-19,42]

Agent	FDA Indication(s) [d]	Dosing and administration[ab]
Actemra® (tocilizumab) intravenous infusion, subcutaneous injection	IV: CRS (≥2 yrs), PJIA (≥2 yrs), SJIA (≥2 yrs), RA[c] SQ: GCA, PJIA (≥2 yrs), RA	**CRS IV:** patient < 30 kg -12 mg/kg; patient ≥30 kg - 8 mg/kg (wt) IV up to 4 doses with interval between consecutive doses of at least 8 hours, not to exceed 800mg per infusion **GCA SQ**: 162 mg once every week, in combination with a tapering course of glucocorticoids **PJIA IV**: patient < 30 kg - 10 mg/kg every 4 weeks; patient≥30 kg – 8 mg/kg every 4 weeks **PJIA SQ:** patient < 30 kg – 162 mg once every 3 weeks; patient 30 kg or greater – 162 mg once every 2 weeks **RA IV:** 4 mg/kg, increase to 8 mg/kg if needed, every 4 weeks **RA SQ:** patient < 100kg -162 mg SQ eow up to weekly based on clinical response and weight; patient ≥100 kg – 162 mg every week **SJIA IV:** patient <30 kg -12 mg/kg every 2 weeks; patient ≥30 kg - 8 mg/kg every 2 weeks
Cimzia® (certolizumab) subcutaneous injection	AS, CD, PS, PSA, RA	**AS**: 400 mg at day 0 and weeks 2 and 4, then 200 mg eow or 400 mg every 4 weeks **CD:** 400 mg at day 0 and weeks 2 and 4, then 400 mg every 4 weeks **RA,PSA:** 400 mg at day 0 and weeks 2 and 4, then 200 mg eow (maintenance dosing of 400 mg every 4 weeks can be considered) **PS**: 400 mg every other week; for some patients (body weight ≤90 kg) 400 mg at day 0 and weeks 2 and 4, then 200 mg every other week can be considered

Agent	FDA Indication(s) [d]	Dosing and administration[ab]
Cosentyx® (secukinumab) subcutaneous injection	AS, PS, PSA	**PS, PSA with PS:** 300 mg SC at weeks 0, 1, 2, 3, and 4 followed by 300 mg every 4 weeks. Each 300 mg dose is given as 2 subcutaneous injections of 150 mg. **PSA,AS: with loading dose-** 150 mg SC at weeks 0,1,2,3, and 4 and every 4 weeks thereafter (can go up to 300 mg for PSA) **Without loading dose:** 150 mg SC every 4 weeks
Enbrel® (etanercept) subcutaneous injection	AS, PJIA (≥2 yrs), PS (≥4 yrs), PSA, RA	**RA, PSA, AS:** 50 mg weekly **Adult PS:** 50 mg twice weekly for 3 mos, then 50 mg weekly **Pediatric PS, PJIA:** 0.8 mg/kg weekly (max of 50 mg weekly)
Humira® (adalimumab) subcutaneous injection	AS, CD (≥6 yrs), HS, PJIA (≥2 yrs), PS, PSA, RA, UC, Uveitis°	**AS, PSA, RA:** 40 mg eow; those with RA not on methotrexate may increase to 40 mg weekly **HS:** 160 mg on day 1, 80 mg on day 15, then 40 mg every week starting day 19 **Adult CD, UC:** 160 mg on day 1, 80 mg 2 weeks later (day 15), then 40 mg eow starting day 29 **Pediatric CD:** 17kg to <40kg: 80 mg on day 1, 40 mg on day 15, then 20 mg eow starting day 29 ≥40kg: 160 mg on day 1, 80 mg on day 15, then 40 mg eow starting on day 29 **PJIA:** 10kg to <15kg: 10 mg eow 15kg to <30kg: 20 mg eow ≥30kg: 40 mg eow **PS, Uveitis:** 80 mg day 0, then 40 mg eow starting one week after the initial dose
Kevzara® (sarilumab) subcutaneous injection	RA	**RA:** 200 mg once every 2 weeks
Kineret® (anakinra) subcutaneous injection	NOMID, RA	**NOMID:** 1-2 mg/kg daily; maximum 8 mg/kg daily **RA:** 100 mg per day
Olumiant® (baricitinib) Tablet	RA	**RA:** 2 mg per day

Agent	FDA Indication(s) [d]	Dosing and administration[ab]
Orencia® (abatacept) intravenous infusion; subcutaneous injection	PJIA (≥6 yrs, IV; ≥2 yrs SC), PSA, RA	**PSA SC**: 125mg once weekly without the need for an IV loading dose **RA, PSA IV:** Initial dose <60 kg- 500 mg; 60-100 kg-750 mg; >100 kg-1000 mg, dose should be given at 0, 2, and 4 weeks, then every 4 weeks thereafter **RA SC:** 125 mg once weekly, with or without IV loading dose **PJIA IV** (6 years of age and older)**:** <75 kg- 10 mg/kg; >75 kg- same as adult RA/PSA IV dosing noted above not to exceed 1000 mg, dose should be given at 0, 2, and 4 weeks, then every 4 weeks thereafter **PJIA SC** (2 years of age and older): weight based 10 -<25kg: 50 mg weekly; 25-<50kg: 87.5mg weekly; ≥50 kg: 125 mg weekly; without the need for IV loading dose
Siliq™ (brodalumab) subcutaneous injection	PS	**PS:** 210 mg injected at weeks 0,1, and 2, followed by 210mg every 2 weeks
Simponi® (golimumab) subcutaneous injection	AS, PSA, RA, UC	**AS, PSA, and RA**: 50 mg once a month **UC**: initially 200 mg Week 0, followed by 100 mg at Week 2, then 100 mg every 4 weeks
Stelara® (ustekinumab) intravenous infusion; subcutaneous injection	IV: CD (induction therapy only) SQ: CD, PS (≥12 yrs), PSA	**CD IV:** single induction infusion; weight based – up to 55 kg – 260mg; >55 kg to 85 kg – 390 mg; > 85 kg – 520 mg **CD SC:** 90 mg 8 weeks after initial IV induction, then every 8 weeks thereafter **Adolescent PS SC (> 12 years):** <60 kg – 0.75 mg/kg; 60 kg to 100 kg – 45 mg; >100 kg – 90 mg; dose at initial dose, 4 weeks later then every 12 weeks thereafter. **Adult PS SC:** ≤100 kg - 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks; >100 mg – 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks **Adult PSA SC:** 45 mg initially and 4 weeks later, followed by every 12 weeks **PS with PSA SC**: >100 kg - 90 mg initially and 4 weeks later, followed by every 12 weeks
Taltz® (ixekizumab) subcutaneous injection	PS, PSA	**PS**: 160 mg (2 X 80 mg injections) at Week 0, followed by 80 mg at Weeks 2, 4, 6, 8, 10, and 12, then 80 mg every 4 weeks **PSA**: 160 mg (2 x 80 mg injections) at week 0, followed by 80mg every 4 weeks
Tremfya® (guselkumab) subcutaneous injection	PS	**PS:** 100 mg at Week 0, Week 4, and every 8 weeks thereafter

Agent	FDA Indication(s) [d]	Dosing and administration[ab]
Xeljanz® (tofacitinib) oral tablets	PSA, RA, UC	**PSA, RA:** 5 mg orally twice daily **UC**: 10 mg orally twice daily for 8 weeks; then 5 or 10 mg twice daily. Discontinue after 16 weeks of 10mg twice daily, if adequate therapeutic benefit is not achieved
Xeljanz® XR (tofacitinib extended release) oral tablets	PSA, RA	**ALL:** 11 mg orally once daily

AS=Ankylosing Spondylitis, CAPS/NOMID= Cryopyrin Associated Periodic Syndrome/ Neonatal-Onset Multisystem Inflammatory Disease, CD=Crohn's Disease, CRS = Cytokine Release Syndrome, GCA = Giant Cell Arteritis, HS= Hidradenitis Suppurativa, JIA=Juvenile Idiopathic Arthritis, PJIA=Polyarticular Juvenile Idiopathic Arthritis, PS=Psoriasis, PSA=Psoriatic Arthritis, RA=Rheumatoid Arthritis, SJIA=Systemic Juvenile Idiopathic Arthritis, UC=Ulcerative Colitis

a - eow-every other week

b - Concomitant use of abatacept or anakinra with TNF antagonists has been shown to increase the risk of infection without improving efficacy. As a result, FDA labeling recommends against combination therapy of two or more biologics.

c - after inadequate response to one or more disease modifying anti-rheumatic drugs (DMARDs)

d - If age is not specified, label indicates for "adult" patients

° - indicated for the treatment of non-infectious intermediate, posterior and panuveitis in adult patients

POLICY

Note: This policy does not apply to infused drugs.

Prior Authorization and Quantity Limit Criteria for Approval

Initial Evaluation

Targeted agents will be approved when the following are met:

1. ONE of the following:
   A. There is documentation that the patient is currently being treated with the requested agent (starting on samples is not approvable)
   (evidence of a paid claim within the past 90 days, or patient is new to the claim system within the past 120 days **and** a physician states the patient is currently taking the requested medication in the past 90 days [starting on samples is not approvable])
   OR
   B. The prescriber states the patient is currently being treated with the requested agent (starting on samples is not approvable) AND is at risk if therapy is changed
   OR

C. ALL of the following:
  i. ONE of the following:
    a. The patient has a diagnosis of rheumatoid arthritis (RA) that is labeled for the requested agent AND ONE of the following:
      1) The patient has tried and had an inadequate response to maximally tolerated methotrexate (e.g., titrated to 25 mg weekly) for at least 3-months
      OR
      2) The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to methotrexate
      OR
      3) The patient has tried and had an inadequate response to another conventional agent (e.g., hydroxychloroquine, leflunomide, or sulfasalazine) used in the treatment of RA for at least 3-months
      OR
      4) The patient has a documented intolerance, FDA labeled contraindication or hypersensitivity to another conventional agent used in the treatment of RA
      OR
      5) The patient's medication history indicates use of another biologic immunomodulator agent that is FDA approved for RA

    OR

    b. The patient has an FDA labeled indication or an indication supported in DrugDex with 1 or 2a level of evidence (or otherwise accepted by client) for the requested agent and route of administration AND ONE of the following:
      1) The patient has tried and had an inadequate response to ONE conventional agent for the required length of therapy*
      OR
      2) The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to at least ONE conventional agent
      OR
      3) The patient's diagnosis does NOT require a conventional agent*
      OR
      4) The patient's medication history indicates use of another biologic immunomodulator agent OR Otezla for the same FDA labeled indication or with a DrugDex 1 or 2a level of evidence indication as the requested agent

    AND

ii. If the client has preferred agents, then ONE of the following:
   a. The requested agent is a preferred agent for the requested indication
      OR
   b. The requested indication does NOT require any preferred agents
      OR
   c. The patient has tried and had an inadequate response to the required amount of preferred agents for the requested indication for at least 3 months (See Preferred Agent AND Try and Fail Column)
      OR
   d. The patient has a documented intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration), FDA labeled contraindication, or hypersensitivity to ALL required preferred agents for the requested indication

   AND

iii. If Stelara 90 mg is requested, ONE of the following:
   a. The patient has a diagnosis of psoriasis AND weighs >100kg AND the patient has tried and had an inadequate response to Stelara 45mg for at least 3 months
      OR
   b. The patient has a dual diagnosis of psoriasis AND psoriatic arthritis AND the patient is >100kg
      OR
   c. The patient has a diagnosis of Crohn's disease

AND

2. The prescriber is a specialist in the area of the patient's requested indication or has consulted with a specialist in the area of the patient's requested indication (e.g. rheumatologist for JIA, PsA, RA; gastroenterologist for CD, UC; dermatologist for PS; oncologist for CRS)

   AND

3. ONE of the following:
   A. The patient is NOT currently being treated with another biologic immunomodulator agent or Otezla
      OR
   B. The patient is currently being treated with another biologic immunomodulator agent or Otezla AND will discontinue prior to starting the requested agent

   AND

4. The patient does NOT have any FDA labeled contraindication(s) to the requested agent

   AND

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

   AND

6. ONE of the following:
   A. The quantity (dose) requested is within the program quantity limit
      OR
   B. The quantity (dose) requested is greater than the program quantity limit and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis

*****NOTE: Conventional agent required for diagnoses of ankylosing spondylitis, Crohn's disease, giant cell arteritis, hidradenitis suppurative, polyarticular juvenile idiopathic arthritis, psoriatic arthritis, psoriasis, rheumatoid arthritis, systemic juvenile idiopathic arthritis, ulcerative colitis, and uveitis.

Length of approval:

- 12 months for all agents EXCEPT Humira (adalimumab) for ulcerative colitis (UC), Siliq for plaque psoriasis (PS), Xeljanz for UC, and the agents with indications that require loading doses for new starts. For agents that require a loading dose for a new start, approve the loading dose noted in the table AND the maintenance dose for the remainder of the 12 months.
- Humira for UC may be approved for 12 weeks.
- Siliq for PS for 16 weeks.
- Xeljanz for UC may be approved for 16 weeks.

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

Renewal Evaluation

Targeted agents will be approved when the following are met:

1. The patient has been previously approved for the requested agent through Prime Therapeutics PA process (*please note Stelara renewal must be for the same strength as the initial approval)
   AND
2. The patient has shown clinical improvement with the requested agent (i.e. slowing of disease progression or decrease in symptom severity and/or frequency)
   AND
3. The prescriber is a specialist in the area of the patient's requested indication or has consulted with a specialist in the area of the patient's requested indication (e.g. rheumatologist for JIA, PsA, RA; gastroenterologist for CD, UC; dermatologist for PS; oncologist for CRS)
   AND

4. ONE of the following:
   A. The patient is NOT currently being treated with another biologic immunomodulator agent or Otezla
      OR
   B. The patient is currently being treated with another biologic immunomodulator or Otezla AND will discontinue prior to continuing the requested agent

   AND
5. The patient does NOT have any FDA labeled contraindication(s) to the requested agent

   AND
6. ONE of the following:
   A. The quantity (dose) requested is within the program quantity limit
      OR
   B. The quantity (dose) requested is greater than the program quantity limit AND the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist

Length of approval: 12 months

Indication	Conventional Agent Prerequisites	Trial Length
Rheumatoid Disorders		
Ankylosing spondylitis	Two different NSAIDs Accept but do not offer: sulfasalazine	4 weeks total trial
Polyarticular juvenile idiopathic arthritis (PJIA)	Leflunomide methotrexate NSAID (ibuprofen, naproxen, indomethacin) sulfasalazine Accept but do not offer: azathioprine, cyclosporine, intra-articular glucocorticoids	3 months, except NSAID use is accepted for 1 month
Psoriatic arthritis (PSA)	Hydroxychloroquine leflunomide methotrexate minocycline sulfasalazine	3 months
Rheumatoid arthritis (RA)	Hydroxychloroquine leflunomide methotrexate sulfasalazine	3 months

Indication	Conventional Agent Prerequisites	Trial Length
Systemic juvenile idiopathic arthritis (SJIA)	Leflunomide methotrexate COX-2 (celecoxib) NSAID (must have had minimum 1 month trial) Oral glucocorticoid Accept but do not offer: azathioprine, chlorambucil, cyclophosphamide, cyclosporine, etoposide, tacrolimus, thalidomide,	3 months, except NSAID use is accepted for 1 month
Dermatological Disorders		
Hidradenitis suppurative (HS)	Oral tetracyclines (doxycycline, tetracycline) oral contraceptives (females only) intralesional corticosteroids (triamcinolone, dexamethasone, betamethasone) Accept but do not offer: oral retinoids (acitretin, isotretinoin), finasteride, spironolactone,	3 months
Psoriasis (PS)	acitretin anthralin calcipotriene calcitriol coal tar products cyclosporine methotrexate methoxsalen pimecrolimus PUVA (phototherapy) tacrolimus tazarotene topical corticosteroids	3 months
Inflammatory Bowel Disease		
Crohn's disease (CD)	6-mercaptopurine aminosalicylates azathioprine corticosteroids (including prednisone, budesonide EC capsule) mesalamine methotrexate sulfasalazine	3 months
Ulcerative colitis (UC)	6-mercaptopurine azathioprine balsalazide corticosteroids cyclosporine metronidazole mesalamine steroid suppositories sulfasalazine	3 months

Indication	Conventional Agent Prerequisites	Trial Length
Other		
Uveitis (Please note: a diagnosis must be non-infectious intermediate, posterior, or panuveitis uveitis)	Difluprednate periocular injection of a glucocorticoid (e.g. triamcinolone 40mg) intraocular injection of a glucocorticoid (e.g. Triesence/triamcinolone 4mg or Ozurdex/dexamethasone implant) oral prednisone (approximately 40-60mg/day or 1 mg/kg/day) Accept but do not offer: azathioprine, mycophenolate, methotrexate, cyclosporine, tacrolimus, cyclophosphamide	2 weeks 1 time injection 2 weeks
Giant Cell Arteritis (GCA)	Systemic corticosteroid therapy (e.g., prednisone, methylprednisolone)	7-10 days
Cytokine Release Syndrome (CRS)	None required	N/A
Neonatal Onset Multisystem Inflammatory Disease (NOMID)	None required	N/A

Agents Contraindicated as Concomitant Therapy		
▪ Actemra (tocilizumab) ▪ Arcalyst [a] (rilonacept) ▪ Cimzia (certolizumab) ▪ Cosentyx (secukinumab) ▪ Enbrel (etanercept) ▪ Entyvio (vedolizumab) ▪ Humira (adalimumab) ▪ Ilaris [a] (canakinumab)	▪ Inflectra (infliximab-dyyb) ▪ Kevzara (sarilumab) ▪ Kineret (anakinra) ▪ Olumiant (baricitinib) ▪ Orencia (abatacept) ▪ Otezla (apremilast) ▪ Remicade (infliximab) ▪ Renflexis (infliximab-abda) ▪ Siliq (brodalumab)	▪ Simponi (golimumab) ▪ Simponi ARIA (golimumab) ▪ Stelara (ustekinumab) ▪ Taltz (ixekizumab) ▪ Tremfya (guselkumab) ▪ Tysabri [a] (natalizumab) ▪ Xeljanz (tofacitinib) ▪ Xeljanz XR (tofacitinib extended release)

[a] – Arcalyst (rilonacept), Ilaris (canakinumab), and Tysabri (natalizumab) are not targets in this program but will be included as a biologic immunomodulator contraindicated in the 30-day washout period.

Agent	FDA Labeled Contraindication(s)
Actemra (tocilizumab)	Known hypersensitivity to Actemra
Cimzia (certolizumab)	Serious hypersensivity reaction to certolizumab pegol or to any of the excipients
Cosentyx (secukinumab)	Serious hypersensitivity reaction to secukinumab or to any of the excipients
Enbrel (etanercept)	Sepsis
Humira (adalimumab)	None
Kevzara (sarilumab)	Known hypersensitivity to sarilumab or any of the inactive ingredients
Kineret (anakinra)	Hypersensitivity to *E coli* proteins
Olumiant (baricitinib)	None
Orencia (abatacept)	None
Siliq (brodalumab)	Crohn's disease

Agent	FDA Labeled Contraindication(s)
Simponi (golimumab)	None
Stelara (ustekinumab)	Clinically significant hypersensitivity to ustekinumab or to any of the excipients
Taltz (ixekizumab)	Serious hypersensitivity reaction, to ixekizumab or to any of the excipients
Tremfya (guselkumab)	None
Xeljanz (tofacitinib) Xeljanz XR (tofacitinib extended-release)	None

Brand (generic)	Quantity Limit
Actemra® (tocilizumab)	
162 mg/0.9 mL syringe	4 syringes (3.6 mL)/28 days
Cimzia® (certolizumab)	
2 x 200 mg/mL syringe, kit	2 kits/28 days
6 X 200 mg/mL syringe, starter kit	1 starter kit (3)/180 days
Cosentyx™ (secukinumab)****	
300 mg/2 mL (2 x 150 mg/Ml pen	2 pens/28 days
150 mg/mL pen	1 pen/28 days
150 mg/mL syringe	1 syringe/28 days
300 mg/2 mL (2 x 150 mg/mL) syringe	2 syringes/28 days
Enbrel® (etanercept)	
25 mg/vial, kit	8 vials/28 days
50 mg/mL SureClick autoinjector	4 autoinjectors (3.92 mL)/28 days
50 mg/mL Mini injector cartridge	4 cartridges (3.92 mL)/28 days
25 mg/0.5 mL syringe	4syringes (2.04) mL)/28 days
50 mg/mL syringe	4 syringes (3.92 mL)/28 days
Humira® (adalimumab)++	
10 mg/0.1 mL syringe	2 syringes/28 days
10 mg/0.2 mL syringe	2 syringes/28 days
20 mg/0.2 mL syringe	2 syringes/28 days
20 mg/0.4 mL syringe, kit	2 syringes/28 days
Pediatric Crohn's Starter Kit 40 mg/0.8mL (Both 3 and 6 syringe pack)	1 kit/180 days [1 kit (3 syringes) 1 kit (6 syringes)]
40 mg/0.8 mL syringe, kit	2 syringes/28 days
40/0.4 mL syringe	2 syringes/28 days
Pediatric Crohn's Disease Starter kit (80 mg/0.8 mL syringe)	1 kit (3 syringes)/180 days
Pediatric Crohn's Disease Starter kit (40 mg/0.4 mL and 80 mg/0.8 mL syringe)	1 kit (2 syringes)/180 days
40 mg/0.8 mL pen, kit	2 pens (kits)/28 days
Psoriasis, Uveitis Starter kit 40 mg/0.8 mL pen	1 kit (4 pens)/180 days
Crohn's Disease, Ulcerative Colitis, or Hidradenitis Starter kit 40 mg/0.8 mL pen	1 kit (6 pens)/180 days
40 mg/0.4 mL pen	2 pens/28 days
80 mg/0.8 mL pen, Crohn's disease, ulcerative colitis, or hidradenitis suppurtaiva Starter kit	1 kit (3 pens)/180 days
80 mg/0.8 mL and 40 mg/0.4 mL pen, Psoriasis, uveitis Starter kit	1 kit (3 pens)/180 days

Brand (generic)	Quantity Limit
Kevzara (sarilumab)	
150 mg/1.14 mL pen	2 pens (2.28 mL)/28 days
200 mg/1.14 mL pen	2 pens (2.28 mL)/28 days
150 mg/1.14 Ml syringe	2 syringes (2.28 mL)/28 days
200 mg/1.14 Ml syringe	2 syringes (2.28 mL)/28 days
Kineret® (anakinra)	
100 mg syringe	28 syringes (18.76 mL)/28 days
Olumiant (baricitinib)	
2 mg tablets	1 tablet/day
Orencia® (abatacept)	
50 mg/0.4 mL syringe	4 syringes (1.6 mL)/28 days
87.5 mg/ 0.7 mL syringe	4 syringes (2.8 mL)/28 days
125 mg/mL syringe	4 syringes (4 mL)/28 days
125 mg/mL ClickJect autoinjector	4 autoinjectors/28 days
Siliq (brodalumab)^	
210 mg/1.5 mL syringe	2 syringes (3 mL)/28 days
Simponi® (golimumab)**	
50 mg/0.5 mL auto-injector	1 auto-injector (0.5 mL)/28 days
50 mg/0.5 mL syringe	1 syringe (0.5 mL)//28 days
100 mg/1 mL auto-injector	1 auto-injector (1 mL)/28 days
100 mg/1 mL syringe	1 syringe (1 mL)/28 days
Stelara (ustekinumab)***	
45 mg/0.5 mL vial	1 vial (0.5 mL)/84 days
45 mg/0.5 mL syringe	1 syringe (0.5 mL)/84 days
90 mg/1 mL syringe	1 syringe (1 mL) /56 days
Taltz (ixekizumab)*****	
80 mg/mL autoinjector	1 syringe/28 days
80 mg/mL syringe	1 syringe/28 days
Tremfya (guselkumab)^^	
100 mg/mL syringe	1 syringe/56 days
Xeljanz® (tofactinib)	
5 mg tablet	2 tablets/day
10 mg tablet	2 tablets/day
Xeljanz XR® (tofactinib extended release)	
11 mg tablet	1 tablet/day

*- Enbrel 50mg may be approved for twice weekly (8 syringes/28 days) dosing for the first 3 months for a diagnosis of psoriasis.
++- Humira may be approved for higher than the QL for HS and RA (those patients not on methotrexate) only.
**- Simponi 200mg on week 0, 100mg on week 2 may be approved for a diagnosis of ulcerative colitis.
***- Stelara 45mg/0.5mL may be approved for patients who are <100 kg on weeks 0, 4, and every 12 weeks thereafter for a diagnosis of plaque psoriasis. Stelara 90mg/1mL may be approved for patients >100kg on weeks 0, 4 and every 12 weeks thereafter for a diagnosis of plaque psoriasis.
**** - Up to 10 syringes will be allowed for the first month for dose titration followed by 2 syringes per 28 days afterwards.
*****- Taltz 160 mg (2 X 80 mg injections) SC at Week 0, followed by 80 mg at Weeks 2, 4, 6, 8, 10, and 12, then 80 mg every 4 weeks thereafter
^- Siliq 210 mg Week 0, 1, and 2 followed by 210 mg every 2 weeks
^^- Tremfya 100mg Week 0, Week 4, and then every 8 weeks thereafter

RATIONALE

RHEUMATOID DISORDERS

Ankylosing spondylitis (AS)

Ankylosing spondylitis (AS) is a form of chronic inflammatory arthritis characterized by sacroiliitis, enthesitis, and a marked propensity for sacroiliac joint and spinal fusion. AS is distinguished with universal involvement with sacroiliac joint inflammation or fusion and more prevalent spinal ankylosis. Goals of treatment for AS are to reduce symptoms, maintain spinal flexibility and normal posture, reduce functional limitations, maintain work ability, and decreases disease complications.[20] The mainstay of treatment has been NSAIDs and exercise, with the additional use of DMARDs in patients with peripheral arthritis.[20,21] The ACR, Spondylitis Association of America (SAA), and Spondyloarthritis Research and Treatment Network (SPARTAN) recommends the following pharmacological for treatment of AS:[21]

- Stable AS: First line therapy with on demand NSAIDs; there is also a conditional recommendation for continuation of TNF inhibitor as monotherapy
- Active AS:
  - First line therapy with continuous NSAIDs and TNF inhibitor if active AS despite NSAIDS
    - Lack of response (or intolerance) to at least 2 different NSAIDs over 1 month or incomplete response to at least 2 different NSAIDs over 2 months would be an adequate NSAID trial to judge response
  - DMARDs (methotrexate, sulfasalazine, leflunomide, pamidronate, thalidomide, apremilast) are not recommended unless patient has failed NSAID and have contraindication to TNF-inhibitor
  - If patient has concomitant inflammatory bowel disease or recurrent iritis, TNF-inhibitors, such as infliximab or adalimumab, are recommended over etanercept. If disease activity continues, despite adding a TNF, switch to a different TNF inhibitor.
  - Glucocorticoids are not recommended, but may be considered in the event of polyarticular flare of peripheral arthritis, IBD flares, or flares during pregnancy.

Rheumatoid arthritis (RA)

Treatment of RA is directed towards the control of synovitis and the prevention of joint injury. The choice of therapy depends on several factors, including the severity of disease activity when therapy is initiated and the response of the patient to prior therapeutic interventions. Treatment strategies include approaches directed at achieving remission or low disease activity by more rapid and sustained control of inflammation by disease-modifying anti-rheumatic drug (DMARD) therapy early in the disease course.[22]

American College of Rheumatology (ACR) guidelines recommend a treat-to-target approach in therapy, regardless of disease activity. Treatment goals are for low disease activity or remission. ACR guidelines categorize therapy for those with early RA (disease duration <6 months) or established RA (disease duration ≥6 months) as follows:[23]

- For early RA patients, the ACR recommends the following:
  - Naïve to therapy, DMARDs, methotrexate (MTX), as initial, monotherapy therapy unless contraindicated. Other DMARD monotherapy options include sulfasalazine, hydroxychloroquine, and leflunomide.

    - Moderate or high disease activity despite DMARD, treatment with combination DMARDs or a TNF-inhibitor (adalimumab, cetolizumab pegol, etanercept, golimumab, or infliximab) or a non-TNF inhibitor (abatacept, rituximab, or tocilizumab (excludes anakinra)), with or without MTX.
    - Moderate or high disease activity despite the previous DMARD or biologic therapy, addition of low-dose glucocorticoid (≤10 mg/day of prednisone or equivalent) to bridge therapy until therapeutic effects of DMARD is reached. ACR also recommends short-term (< 3 months) with lowest dose of glucocorticoids for flares.
- For established RA patients, the ACR recommends the following:
    - Low disease activity and is DMARD naïve, DMARD monotherapy is recommended over a TNF-inhibitor.
    - Moderate or high disease and is DMARD naïve, DMARD monotherapy is recommended over double or triple DMARD therapy and tofacitnib.
    - In general, MTX is preferred initial therapy for most patients with established RA with active disease.
    - Moderate-high disease activity despite DMARD monotherapy, combination DMARD therapy OR the addition of TNF inhibitor, non-TNF biologic, or tofacitinib with or without MTX is recommended rather than continuing DMARD monotherapy. Combination biologic therapy and MTX is recommended over biologic monotherapy.
    - Moderate or high disease despite TNF-inhibitor and not on DMARD, addition of one or two DMARD, rather than TNF-inhibitor monotherapy
    - Moderate or high disease despite TNF-inhibitor, switching to a non-TNF inhibitor, tofacitinib with or without MTX

Early use of DMARD, particularly MTX is recommended as soon as possible following diagnosis of RA.[22] Dosing of MTX for RA is once weekly dosing with starting doses at 7.5 mg or 15 mg once weekly, depending on the degree of disease, size and age of the patient, presence of comorbidities, and renal function. MTX dose is increased as tolerated and as needed to control symptoms and signs of RA disease. The usual target dose is at least 15 mg weekly and the usual maximum dose is 25 mg weekly.[24] ACR defines optimal dosing for RA treatments as 1) dosing to achieve a therapeutic target derived from mutual patient-clinician consideration of patient priorities and 2) given for at least 3 months before therapy escalation or switching.[21] For patients who are unable to take MTX, hydroxychloroquine, sulfasalazine, or leflunomide are other DMARD options.In patients resistant to initial MTX treatment, combination DMARD (e.g. MTX plus sulfasalazine or hydroxychloroquine or a TNF-inhibitor) is recommended.[22]

For patients who are resistant to MTX after 3 to 6 months of treatment at optimal doses (usually 25 mg per week), it is recommended to either use DMARD triple therapy with MTX plus sulfasalazine and hydroxychloroquine or combination of MTX with TNF inhibitor. Triple therapy regimen has been found to be of similar clinical efficacy to MTX with biologics in several randomized trials, including in patients with high level of disease activity or with adverse prognostic features. The use of triple therapy has been shown to be highly cost-effective compared with combining a biologic with MTX, providing comparable or near comparable clinical benefit. The use of biologic with MTX combination is preferred when patients have high disease activity and clinical benefit from a more rapid response is needed and when patients who do not

achieve satisfactory response within 3 to 6 months with non-biologic triple therapy following an inadequate response to MTX therapy.[25]

Polyarticular Juvenile Idiopathic Arthritis (PJIA)

Polyarticular juvenile idiopathic arthritis (PJIA) was formerly called polyarticular onset juvenile rheumatoid arthritis. PJIA is a subset of juvenile idiopathic arthritis (JIA) that is defined by the presence of more than four affected joints during the first 6 months of illness. Therapy is directed toward treating the underlying inflammation of JIA and preventing complications associated with JIA (e.g. joint damage) or the adverse effects of its treatment. First line agents for PJIA include nonsteroidal antiinflammatory drugs (NSAIDs) and nonbiologic DMARDs such as methotrexate. MTX has been a standard therapy for PJIA taking 6 to 8 weeks until benefits are demonstrated. Sulfasalazine and leflunomide are additional DMARDs that maybe useful in patients with contraindications to MTX. Second line drugs for PJIA are biologic DMARDs, which include TNF-alpha agents (e.g. adalimumab, etanercept, infliximab). Intra-articular glucocorticoids are also a treatment option for PJIA but the need for repeated injections in the same joints or multiple joints simultaneously may not be ideal for the patient population. For children with active disease despite appropriate treatment with NSAIDs and MTX, azathioprine and cyclosporine have been used with varying success. However, these drugs carry significant potential toxicity and appear to be less effective than newer biologic agents.[26]

Systemic Juvenile Idiopathic Arthritis (SJIA)

Systemic juvenile idiopathic arthritis (SJIA) was formerly called Still's disease or juvenile rheumatoid arthritis. It is a subset of JIA that is characterized by daily quotidian fever, rash, and arthritis.[25] The American College of Rheumatology (ACR) defines SJIA as arthritis in ≥1 joint for at least 6 weeks' duration in a child age < 16 years with or preceded by fever of at least 2 weeks' duration that is documented to be daily ("quotidian") for at least 3 days and accompanied by one or more of the following: evanescent erythematous rash, generalized lymphadenopathy, hepatomegaly or splenomegaly, and serositis.[27]

Goals of therapy for SJIA includes control of active inflammation and symptoms and the prevention of a number of disease and/or treatment related morbidities, such as growth disturbances, joint damage, and functional limitations. SJIA initial therapy treatment update for active systemic features includes NSAIDs, systemic glucocorticoids (oral or intravenous) and anakinra (IL-1). Many children with SJIA have refractory disease, in which agents targeting interleukins IL-1 and IL-6 are used. ACR suggests continued disease activity be managed with calcineurin inhibitors, canakinumab (IL-1), tocilizumab (IL-6), TNF-α inhibitors, methotrexate, leflunomide or options included in initial therapy not yet utilized. Treatment suggestions/decisions are based on the patient's physician global assessment (MD global) and active joint count (AJC).[27]

Treatment with NSAID as monotherapy is effective for some children with treatment length of no more than a few weeks. Glucocorticoids along with DMARD, methotrexate, were traditionally used in patients who failed NSAID therapy. Biologic DMARDs, IL-1 and II-6, were initially reserved for patients refractory to conventional therapy (NSAIDs followed by the addition of glucocorticoids with or without methotrexate).[28]

Psoriatic Arthritis (PsA)

Treatment goals of psoriatic arthritis (PsA) aim to control inflammation and preventing discomfort, joint damage, and disability. Treatment involves the use of a variety of interventions, including many agents used for the treatment of other inflammatory arthritis, particularly spondyloarthritis and RA, and other management strategies of the cutaneous manifestations of psoriasis.[29]

Choice of therapy for peripheral arthritis is based upon the severity of disease and patient's response to treatment. For mild arthritis, NSAIDs are recommended. For moderate to severe arthritis or for patients resistant to initial NSAIDs, DMARDs such as MTX or leflunomide are recommended. Alternative DMARDs include sulfasalazine, antimalarials, and azathioprine. Use of biologic DMARD can be employed for the treatment of other disease manifestations. Patients presenting with severe disease, such as many involved joints, erosive disease at presentation, and functional limitation, biologics are recommended as first line therapy. Patients typically require up to 3 months of therapy to achieve a maximal response.[29]

Choice of therapy for axial disease (involving the sacroiliac joints and spine) is based upon the severity of disease and the patient's response to treatment. Mild symptoms can be treated with NSAID, while moderate to severe arthritis or who are resistant to NSAIDs alone are usually treated with a biologic DMARD. Conventional DMARD, such as MTX, recommended and is the most commonly used first-line DMARD, prior to biologic therapy. Alternative conventional DMARDs, include leflunomide, sulfasalazine, azathioprine, antimalarials or cyclosporine, can be used in patients who are resistant to or intolerant to standard therapy. Oral glucocorticoids in PsA are generally avoided since their use is associated with an increased chance of developing erythroderma or pustular psoriasis.[29]

DERMATOLOGICAL DISORDERS

Psoriasis (PS)

Psoriasis (PS) is a chronic inflammatory skin condition that is often associated with systemic manifestations, especially arthritis. Diagnosis is usually clinical, based on the presence of typical erythematous scaly patches, papules, and plaques that are often pruritic and sometimes painful. Approximately 90% of affected patients have plaque psoriasis, characterized by well-defined round or oval plaques that differ in size and often coalesce. Plaque psoriasis lesions occur on inframmary, axillary, inguinal and intergluteal areas. Heat, trauma, and infection may contribute to its development. Psoriatic arthritis is a seronegative inflammatory arthritis with various clinical presentation including established inflammatory articular disease, active psoriasis, typical psoriatic nail dystrophy, and swelling of an entire digit.[30]

Treatment goals for psoriasis include improvement of skin, nail, and joint lesions plus enhanced quality of life. Patients can be grouped into mild to moderate (less than 5% of body surface area (BSA)) and moderate to severe (5% or more of BSA) disease categories. Limited or mild to moderate, skin disease can often be managed with intermittent topical agents such as topical corticosteroids, vitamin D analogs (calcipotriene and calcitriol), and calcineurin inhibitors (tacrolimus and pimecrolimus). Less commonly used topical therapies include non-medicated moisturizers, salicylic acid, coal tar, and anthralin. Systemic reviews have concluded that more potent agents produce greater improvements in psoriasis symptoms. Vitamin D analogs are used as monotherapy or in combination with phototherapy for psoriasis in patients with 5 to 20% BSA

involvement. These agents have a slower onset of action but a longer disease-free interval than topical corticosteroids.[30] Patient's with more severe psoriasis (more than 5% of BSA or involving hands, feet, face or genitals) are generally treated with phototherapy in combination with systemic therapies. Systemic therapies include methotrexate, cyclosporine, acitretin, apremilast, and biologic therapies.[30,31]

Primary treatment for scalp psoriasis is topical corticosteroids. Combining corticosteroid and a vitamin D analog may offer additional benefits. Other topical therapies used are tazarotene, coal tar shampoo, anthralin, and intralesional corticosteroid injections. Salicyclic acid can be helpful as adjunctive treatment because of its keratolytic effective. Phototherapy and systemic agents are additional options for patients who cannot achieve sufficient improvement with topical agents.[30]

Hidradenitis Suppurativa (HS)

Hidradenitis suppurativa (HS) is a chronic, painful, follicular occlusive disease that affects the folliculopilosebaeceous unit, mainly but not exclusively in the intertriginous axillary, groin, perianal, genital, and inframammary skin. The clinical course of HS is highly variable, ranging from relatively mild cases characterized by the recurrent appearance of papules, pustules, and a few inflammatory nodules to severe cases demonstrating deep fluctuant abscesses, draining sinuses, and severe rope-like scars.[32]

Treatment goals for HS include to reduce the frequency of new lesions, minimizing pain, and suppuration; to prevent disease progression by limiting the formation of scarring; to treat existing lesions and scarring, which may require a combination of medical and surgical interventions. Pharmacological treatment includes topical clindamycin, intralesional corticosteroid injections, punch debridement, and topical resorcinol. Topical clindamycin is often first line therapy for mild HS. Short courses of antibiotics (e.g. 7 days) of antibiotics do not appear to alter the natural history of acute HS lesions. Prolonged courses of of an oral tetracycline is recommended for HS. Oral tetracyclines may also be beneficial to prevent or reduce the frequency of new lesions and are a key treatment for mild to moderate HS. Doxycycline, lymecycline, tetracycline, and minocycline can be used and treatment is usually continued for several months. Combination clindamycin and rifampin; dapsone monotherapy; combination dapsone with rifampin, moxifloxacin, and metronidazole; erythromycin; and cephalosporins have shown benefit in HS. Oral retinoids, such as acitretin, isotretinoin, and alitreinoin, have also been used for HS.[32]

For severe and refractory HS, treatment recommendations include TNF-α-inhibitors (adalimumab and infliximab), short courses of prednisone for acute inflammation, and cyclosporine. Adalimumab is the only biologic agent that has FDA approval for HS. Three to four days of prednisone 40mg to 60 mg per day, tapered over 7 to 10 days, is sufficient for acutely managing inflammation.[32]

INFLAMMATORY BOWEL DISEASE

Crohn's Disease (CD)

Crohn's Disease (CD) is an inflammatory condition that can affect any portion of the gastrointestinal tract from the mouth to the perianal area. Choice of therapy is dependent on the anatomic location of disease, the severity of disease, and whether the treatment goal is to induce remission or maintain remission. The American Gastroenterological Association (AGA) guideline recommends the following:[33]

- Induction of remission in moderately severe CD:

  - Systemic corticosteroids with concomitant thiopurine (6-mercaptopurine or azathioprine) or MTX to help maintain the corticosteroid-induced remission.
  - Anti-TNF (infliximab or adalimumab) with thiopurines are recommended in those refractory to standard therapies (mesalamine, antibiotics, corticosteroids and immunomodulators).
- Maintenance of remission in moderately severe CD:
  - Following steroid-induced remission, thiopurine or MTX are preferred over no therapy
  - Following steroid induced or anti-TNF drug induced remission, anti-TNF with or without thiopurine to maintain remission is preferred over no therapy

Ulcerative Colitis (UC)

Ulcerative colitis is a chronic inflammatory condition characterized by relapsing and remitting episodes of inflammation limited to the mucosal layer of the colon. It almost invariably involves the rectum and may extend in a proximal and continuous fashion to involve other portions of the colon. Treatment for UC is based on disease severity and extent.[34] AGA recommends the following based on colectomy risk:[35]

- Low risk:
  - Inductive therapy: oral 5-ASA and/or rectal 5-ASA (first line therapy in distal UC), or oral budesonide or prednisone and/or rectal steroids
  - Maintenance therapy: oral 5-ASA and/or rectal 5-ASA; taper steroid over 60 days
- High risk, outpatient (3 options):
  - Inductive therapy: short course of steroids with initiation of thiopurine; Maintenance therapy with thiopurine and taper steroids over 60 days OR Anti-TNF ± thiopurine OR vedolizumab ± thiopurine/MTX
  - Inductive therapy: Anti-TNF ± thiopurine; Maintenance with continued anti-TNF ± thiopurine
  - Inductive therapy: vedolizumab ± immunomodulator; Maintenance with continued vedolizumab ± immunomodulator
- High risk, inpatient (3 options):
  - Induction therapy: IV steroids; Maintenance with thiopurine, anti-TNF ± thiopurine, or vedolizumab ± immunomodulator
  - Induction therapy: infliximab; Maintenance with infliximab ± thiopurine
  - Induction therapy: IV cyclosporine; Maintenance with thiopurine, anti-TNF ± thiopurine, or vedolizumab ± immunomodulator

For initial therapy, combination therapy of oral 5-ASA and rectal 5-ASA for 4 to 8 weeks has been shown to have higher remissions rates than oral mesalamine alone. For patients with mild to moderate UC who do not tolerate or have inadequate response to combination oral 5-ASA and topical 5-ASA or steroids within 2 to 4 weeks, multimatris (MMX) budesonide is recommended for 8 weeks prior to the use of other oral glucocorticoids. Oral glucocorticoids are highly effective in inducing remission in patients with active UC. Prednisone is usually effective within 10 to 14 days, after which the dose can be tapered gradually. Maintenance therapy is recommended in all patients with life-sided colitis, pancolitis, or extensive colitis. 5-ASA medications are highly effective in the maintenance of remission in patients with UC. After an adequate clinical response and/or remission has been achieved, usually in 6 to 8 weeks, oral 5-ASA should be continued to maintain remission.[34]

For severe presentations of UC, initial treatment includes oral glucocorticoids with a combination of high dose 5-ASA and topical therapy with 5-ASA or steroids. Antibiotics are an option for some patients (e.g. ciprofloxacin and metronidazole) is recommended in patients with severe colitis and high-grade fever, leukocytosis with extreme immature neutrophils, and peritoneal signs or megacolon. There is no role of antibiotics in patients with severe colitis without signs of systemic toxicity. Patients who continue to have symptoms despite optimal doses of oral steroids, high dose oral 5-ASA, and topical 5-ASA/steroids should be hospitalized for further management that includes intravenous fluids, electrolyte repletion, and intravenous steroids. Intravenous cyclosporine has a role with induction of remission in patients with severe or fulminant colitis but is not effective and/or safe for long-term use. It is used as bridge therapy with slower onset medications including azathioprine (AZA) or 6-mercaptopurine (6-MP). Infliximab can induce remission rapidly and can be used for maintenance of remission. However, it is unclear if anti-TNF therapy can prevent or reduce the rates of colectomy in the long term. Infliximab is recommended in patients with an allergy to AZA and 6-MP or who have failed therapy with AZA/6-MP.[35]

Anti-TNF therapy (e.g. infliximab, adalimumab, golimumab) has shown to induce and maintain remission in patients with moderate to severe UC and is recommended to be considered patients who have failed or have an allergy to AZA or 6-MP, or in those patients who cannot wait the anticipated 3 to 6 months for full therapeutic effect.[36]

OTHER DISORDERS

Uveitis

Uvetitis is characterized by inflammation of the uvea, which is the middle portion of the eye. Uveitis frequently occurs in association with other systemic medical conditions, especially infections and inflammatory disease, but may occur as an isolated process.[36] Treatment of non-infectious uveitis depends on the location of inflammation. Anterior uveitis is generally treated with topical glucocorticoids, such as prednisolone ophthalmic drops. Uveitis that is primarily posterior to the lens is generally not responsive to topical medication, although some experts are increasingly using difluprednate. Intraocular and periocular injections of triamcinolone or glucocorticoids are also options, although patients may decline the injections. Systemic treatment is generally reserved for resistant inflammation and maybe indicated in patients with glaucoma who cannot be treated with local injection. Systemic glucocorticoid therapy or additional anti-inflammatory or immunosuppressive agents such as antimetabolites (methotrexate, azathioprine, mycophenolate) and/or calcineurin antagonist (cyclosporine or tacrolimus) can be used to treat uveitis. If remission has been achieved for 6 to 12 months with systemic glucocorticoids, the maintenance dose maybe gradually discontinued. TNF-inhibitors, such as adalimumab, switching to a different agent, or combination of antimetabolite with a calcineurin antagonist is recommended if the patient is unresponsive to first line therapy.[38]

Giant Cell Arteritis (GCA)

Giant cell arteritis (GCA) is also known as Horton disease, cranial arteritis, and temporal arteritis. It is the most common vasculitis in North American and Europe. Many of the clinical features of GCA result from vascular inflammation of the small extracranial branches of the carotid arteries. High-dose systemic glucocorticoids is the mainstay of therapy for GCA. Indications for the addition of a glucocorticoid-sparing agents includes presence of significant premorbid disease, emergence of significant glucocorticoid-related side effects during treatment, or a relapsing

course necessitating protracted glucocorticoid use. Methotrexate or tocilizumab are recommended options for glucocorticoid sparing agents.[40]

Cryopyrin-Associated Periodic Syndromes (CAPS)

Cryopyrin- associated periodic syndromes (CAPS) consists of three very rare diseases related to a defect in the same protein – cryopyrin. All 3 cryopyrinopathies arise from mutations in a single gene, *NLRP3,* encoding a protein called cryopyrin. These diseases differ in the systems involved and in the severity of the disease. Familial cold autoinflammatory syndrome (FCAS) is more common in the United States and Muckle-Wells syndrome (MWS) is more common in Europe. Neonatal-onset multisystem inflammatory disease (NOMID) is the least common disease, usually starting shortly after birth, and is the most severe form.[40,41]

FCAS, formerly called familial cold urticaria, is the mildest of the cryopyrin-associated disorders. Exposure to cold, such as air-conditioned room, results in stereotyped systemic inflammatory response, including fever, an urticarial rash, conjunctival injection, and substantial arthralgias. Symptoms develop with the first year of life, occasionally in the newborn period upon exposure to cold in the delivery room. Attacks resolve within 24 hours, though considerable variability is observed between individuals and depends on the extent and duration of cold exposure. The presence of conjunctivitis and triggering by cold help to discriminate FCAS from other periodic fever disorders. Diagnosis of CAPS is confirmed by genetic testing for *NALP3* mutation and two of the six parameters: urticaria-like rash, cold-triggered episodes, sensorineural hearing loss, musculoskeletal symptoms, chronic aseptic meningitis, and skeletal abnormalities.[41]

MWS is a rare condition characterized by intermittent episodes of fever, headache, urticarial rash, and joint pain (arthralgia or arthritis); progressive sensorineural hearing loss; and secondary amyloidosis with nephropathy. Febrile episodes occur at irregular intervals every few weeks, lasting 12 to 36 hours before resolving spontaneously. Age of onset is variable. Precipitating factors vary and cannot be identified, but they may include both heat and cold. Sensorineural hearing loss, presumably related to inflammation within the cochlea or the leptomeninges, begins in childhood and maybe profound. *NLRP3* mutations implicated in MWS maybe distinct or overlap those causing FCAS.[41]

NOMID usually presents as fever with inflammation in multiple organs. Other signs and symptoms include erythematous rash resembling urticaria, chronic meningitis, which can result in headache, blindness, hearing loss or other neurologic problems, uvetitis, and hepatosplenomegaly.[39,40] After 1 year of age, 50% of patients develop joint pain and swelling of the bones surrounding the large joints, especially the knees. Growth delay can occur in NOMID.[41]

Interleukin (IL)-1- beta inhibitors (anakinra, rilonacept, and canakinumab) have shown effectiveness in preventing and alleviating symptoms of CAPS and reducing levels of inflammatory indices, including serum amyloid A. Treatment with non-steroidal anti-inflammatory drugs, disease modifying antirheumatic drugs, and glucocorticoids was only partially effective.[41]

REVISIONS	
07-01-2015	In Title section updated See also policy from Tysabri (natalizumab) to Tysabri (natalizumab) and Lemtrada (alemtuzumab) (IV Multiple Sclerosis Agents)
	In Description section: ▪ Moved "Simponi® (golimumab)" and "Stelara® (ustekinumab)" from the Nonpeferred Biologic Immunomodulators list to the Preferred list; ▪ Added Actemra (tocilizumab) to and removing Entyvio (vedolizumab) from the Nonpreferred list. ▪ Updated FDA Approved Indications and Dosage chart.
	In Policy Section: ▪ Added "Initial Evaluation" and "Renewal Evaluation" ▪ In Item I added "Simponi (golimumab), and Stelara (ustekinumab)" ▪ In Item I added "The patient has an FDA labeled indication for the requested agent AND" ▪ In Item I 2 d added "conventional" ▪ In Item I 2 f added "at least ONE" ▪ In Item I added: "3. If Stelara 90 mg is requested, ONE of the following: a. The patient has a diagnosis of psoriasis AND weighs >100kg AND the patient has failed (had an inadequate response to) a trial of 45mg for at least 36 months OR b. The patient has a dual diagnosis of psoriasis AND psoriatic arthritis AND the patient is >100kg AND 5. The patient does not have any FDA labeled contraindication(s) to therapy with the requested agent AND 6. The patient has been tested for latent TB AND if positive the patient has begun therapy for active TB AND 7. ONE of the following: a. If all other agents in the program, then the prescribed dosage is within the program limit (FDA approved labeled dosage) OR b. The quantity (dose) requested is greater than the maximum dose recommended in FDA approved labeling, and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist" ▪ In NOTE added, "systemic juvenile idiopathic arthritis" ▪ In Length of approval removed "both" added "all" and "EXCEPT Humira (adalimumab) for ulcerative colitis (UC) and Enbrel for plaque psoriasis. Humira for UC may be approved for 12 weeks. Enbrel for plaque psoriasis may be approved for the loading dose for 12 weeks AND FDA labeled maintenance dose for the remaining 9 months." ▪ In Item II added "The patient has an FDA labeled indication for the requested agent AND" In II 2 c 2) a) removed "BOTH", added "TWO of" and "Simponi or Stelara" In Item II added: "3. The patient does not have any FDA labeled contraindication(s) to therapy with the requested agent AND 4.The patient has been tested for latent TB AND if positive the patient has begun therapy for active TB AND 6. ONE of the following: a. If all other agents in the program, then the prescribed dosage is within the program limit (FDA approved labeled dosage) OR b. The quantity (dose) requested is greater than the maximum dose recommended in FDA approved labeling, and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist *NOTE: Conventional agent required for diagnoses of rheumatoid arthritis, juvenile idiopathic arthritis, systemic juvenile idiopathic arthritis, psoriatic arthritis, psoriasis, ulcerative colitis, or Crohn's disease" ▪ In Length of approval added "non-preferred" and added: "Renewal Evaluation Preferred and Nonpreferred Agents will be approved for renewal when the following criteria are met:

REVISIONS	
	1. The patient has been previously approved for therapy through Prime Therapeutics PA process AND 2. The patient has shown clinical improvement (i.e. slowing of disease progression or decrease in symptom severity and/or frequency) AND 3. The patient does not have any FDA labeled contraindication(s) to therapy with the requested agent AND 4. The patient is not currently being treated with another biologic immunomodulator agent AND 5. ONE of the following: a. The prescribed dosage is within the program set limit (FDA approved labeled dosage) OR b. The quantity (dose) requested is greater than the maximum dose recommended in FDA approved labeling, and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist Length of approval: 12 months for all agents." ▪ Added FDA Labeled Indications for Biologic Immunomodulators chart ▪ Updated the Conventional Agent Prerequisites by Indication, Biologic Agent Contraindicated as Concomitant Therapy, and the Quantity Limits charts.
	Rationale section updated
	In Revision section: ▪ Removed Revision notations for: 06-01-2011, 07-19-2011, 11-01-2011, 11-01-2012.
	References updated
09-01-2015	Updated Description section including: indicating Quantity Limits apply to Otezla, and updating the FDA Approved Indications and Dosage chart.
	In Policy section: ▪ In Item I 3 a corrected "36 months" to "3 months". ▪ In Preferred Agents Length of approval added "and Stelara for all FDA labeled indications." to read "12 months for all agents EXCEPT Humira (adalimumab) for ulcerative colitis (UC), Enbrel for plaque psoriasis, and Stelara for all FDA labeled indications." and added "Stelara may be approved for the loading dose for 1 month and FDA labeled maintenance dose for the remaining 11 months." ▪ In Nonpreferred Agents Length of approval add "except Entyvio" to read, "12 months for all non-preferred agents except Entyvio" and added "Entyvio may be approved for the loading dose for 2 months AND the FDA labeled maintenance dose every 2 months thereafter for the remaining 10 months." ▪ Updated Quantity Limits Chart
	In Revision section: ▪ Removed Revision information for 12-27-2012, 03-01-2013, 06-07-2013, 12-02-2013.
	References reviewed with no updates needed.
09-01-2015	Published 10-06-2015. Retro-effective to 09-01-2015.
	In Description section: ▪ In the Target Drugs chart removed the asterisks beside the drug names and beside "Quantity limits apply as a benefit restriction." As quantity limits apply to all the target drugs. ▪ Following the Target Drugs list added to the notation "Cosentyx" to read, "Note: The quantity limits for Enbrel 50mg, Stelara, Cosentyx and Simponi are reviewable by Prime Therapeutics. All other quantity limits are considered a benefit restriction and are not reviewable by Prime Therapeutics." ▪ Updated the FDA Approved Indications and Dosage chart related to Cosentyx.
	In Policy Section: ▪ After the Quantity Limits chart added for clarity the following notation: "Note: The quantity limits for Enbrel 50mg, Stelara, Cosentyx and Simponi are reviewable by Prime Therapeutics. All other quantity limits are considered a benefit restriction and are not reviewable by Prime Therapeutics."
01-01-2016	Policy published 12-30-2015. Policy effective 01-01-2016.
	In Description section: ▪ Updated FDA Approved Indications and Dosage chart.
	In Policy section: ▪ In Initial Evaluation Preferred Agents Length of Approval removed "Enbrel for plaque psoriasis", "Stelara for all FDA labeled", "Enbrel for plaque psoriasis may be approved for the loading dose for 12 weeks AND FDA labeled maintenance dose for the remaining 9 months" and "Stelara may be approved for the loading dose for 1 month and FDA labeled maintenance dose for the remaining 11 months" and

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	added “that require loading doses for new starts listed in Table 1 below. For agents that require a loading dose for a new start, approve the loading dose noted in the table and also the maintenance dose for the remainder of the 12 months)” to read ▪ “12 months for all agents EXCEPT Humira (adalimumab) for ulcerative colitis (UC) and the agents with indications that require loading doses for new starts listed in Table 1 below. For agents that require a loading dose for a new start, approve the loading dose noted in the table and also the maintenance dose for the remainder of the 12 months). ▪ Humira for UC may be approved for 12 weeks.” ▪ Added Table 1: Preferred Agents with indications that require loading doses ▪ In Initial Evaluation Nonpreferred Agents Length of Approval removed “Entyvio”, “Entyvio may be approved”, “2 months AND”, “every 2 months thereafter”, and “remaining 10” and added “the agents with indications that require loading doses”, “new starts Listed in table 2 below. For agents that require a”, “a new start, approve”, “loading dose noted in the table and also the” and “remainder of the 12” to read “12 months for all non-preferred agents except the agents with indications that require loading doses for new starts listed in Table 2 below. For agents that require a loading dose for a new start, approve the loading dose noted in the table and also the maintenance dose for the remainder of the 12 months” ▪ Added Table 2: Non-preferred Agents with indications that require loading doses. ▪ Updated FDA Labeled Indications for Biologic Immunomodulators, Conventional Agent Prerequisites by Indication, and Quantity Limit charts.
	Rationale section updated
	References updated
05-01-2016	Published 04-29-2016. Effective 05-01-2016.
	In Description section: ▪ In Target Drugs chart added "*" where quantity limits apply. ▪ In Quantity Limits for Target Drugs Note added "Humira" to read "(Note: The quantity limit for Enbrel 50mg, Humira, Stelara, Cosentyx and Simponi are reviewable by Prime Therapeutics. All other quantity limits are considered a benefit restriction. They are not reviewable by Prime Therapeutics.)" ▪ In FDA Approved Indications and Dosage chart updated Cosentyx (secukinumab) and Kineret (anakinra).
	In Policy Section: ▪ In Table 1: Preferred Agents with indications that require loading doses updated to include references. ▪ In Table 2: Non-preferred Agents with indications that require loading doses and FDA Labeled Indications for Biologic Immunomodulators chart updated for Cosentyx (secukinumab) ▪ Added Contraindication chart ▪ In Quantity Limits chart adding added "$^{++}$- Humira may be approved for higher than the QL for HS only." And removed "Note: The quantity limits for Enbrel 50mg, Stelara, Cosentyx and Simponi are reviewable by Prime Therapeutics. All other quantity limits are considered a benefit restriction and are not reviewable by Prime Therapeutics."
07-01-2016	In Description section ▪ Added the new nonpreferred drugs "Taltz (ixekizumab)" and "Xeljanz XR (tofacitinib extended release)" to the FDA Approved Indications and Dosage chart. ▪ In QUANTITY LIMITS FOR TARGET DRUGS added "Taltz" to read "(Note: The quantity limit for Enbrel 50mg, Humira, Stelara, Cosentyx, Simponi, and Taltz are reviewable by Prime Therapeutics. All other quantity limits are considered a benefit restriction. They are not reviewable by Prime Therapeutics.)"
	In Policy section ▪ In Item I 6 added "when required by the prescribing information" to read "The patient has been tested for latent TB when required by the prescribing information AND if positive the patient has begun therapy for active TB" ▪ In Table 2: Non-preferred Agents with indications that require loading doses added "Taltz (ixekizumab)" ▪ Added "Taltz (ixekizumab)" and "and Xeljanz XR (tofacitinib extended-release)" to the following charts: FDA Labeled Indications for Biologic Immunomodulators, Biologic Agent Contraindicated as Concomitant Therapy, and Contraindications.

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	▪ Added "Taltz (ixekizumab)" and "Xeljanz XR (tofacitinib extended-release)" to the Quantity Limits chart as well as the following reference "*****- Taltz 160 mg (2 X 80 mg injections) SC at Week 0, followed by 80 mg at Weeks 2, 4, 6, 8, 10, and 12, then 80 mg every 4 weeks thereafter"
	References updated
07-01-2016	Published 07-20-2016. Retro-effective to 07-01-2016.
	In Policy section - Correction to Nonpreferred Agents ▪ Item 4 added "when required by the prescribing information" to read, "The patient has been tested for latent TB when required by the prescribing information AND if positive the patient has begun therapy for active TB"
07-25-2016	Published 07-20-2016. Effective 07-25-2016.
	In Policy section: Updated policy to allow for increased quantities of Humira for specified indications ▪ In Table 1 and Quantity Limits references added "and RA (those patients not on methotrexate)" to read "++- Humira may be approved for higher than the QL for HS and RA (those patients not on methotrexate) only."
09-01-2016	Description section updated with updates to the FDA Approved Indications and Dosage chart to include the addition of Uveities as an Indication and updates to the key following the chart.
	In Policy section: ▪ In Item I removed "The Preferred Agents Enbrel (etanercept), Humira (adalimumab), Simponi (golimumab), and Stelara (ustekinumab)" and "1. The patient has an FDA labeled indication for the requested agent" ▪ In Item I 2 c added, "ALL of the following: i. The patient has an FDA labeled indication for the requested agent AND ii. ONE of the following:" ▪ In Item I 2 c ii 3) removed "(evidence of a paid claim within the past 180 days, or patient is new to the claim system within the past 120 days and a statement by the physician that the patient has used a prerequisite agent for the intended indication within the past 180 days)" ▪ In Item I 2 c added "iii. If the client has preferred agents, then ONE of the following: 1) The patient's medication history indicates use of TWO of the preferred biologic immunomodulator agents (Enbrel, Humira, Simponi, or Stelara) or the patient has a documented intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration), FDA labeled contraindication, or hypersensitivity to TWO of the preferred agents OR 2) The patient's diagnosis is indicated in only one of the preferred agents and the patient's medication history indicates use of this preferred medication OR the patient has the documented intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration), FDA labeled contraindication, or hypersensitivity to this preferred agent OR 3) The request is for a FDA labeled indication that is not covered by two of the preferred products" ▪ In Item I 2 c vi added "for the requested agent" to read "The patient has been tested for latent TB when required by the prescribing information for the requested agent AND if positive the patient has begun therapy for active TB" ▪ In Item I 3 a removed "If all other agents in the program, then" to read "The prescribed dosage is within the program limit (FDA approved labeled dosage)" ▪ In Item I added "uveitis" to read "*NOTE: Conventional agent required for diagnoses of rheumatoid arthritis, juvenile idiopathic arthritis, systemic juvenile idiopathic arthritis, psoriatic arthritis, psoriasis, ulcerative colitis, uveitis, or Crohn's disease." ▪ Removed "Table 1: Preferred Agents with indications that require loading doses" ▪ Removed criteria for Non-preferred agents "II. Nonpreferred Agents will be approved when the following criteria are met: 1. The patient has an FDA labeled indication for the requested agent AND 2. ONE of the following: a. There is documentation that the patient is currently being treated with the requested agent (evidence of a paid claim within the past 90 days, or patient is new to the claim system within the past 120 days and a physician states the patient is currently taking the requested medication in the past 90 days) OR b. The prescriber states the patient is using the requested agent AND is at risk if therapy is changed OR c. BOTH of the following:

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	1) ONE of the following a) The patient's diagnosis does not require a conventional agent OR b) the patient's medication history indicates the patient has previously failed another biologic immunomodulator agent for the same FDA labeled indication OR c) the patient's medication history indicates use of one conventional agent prerequisite OR d) documented intolerance, FDA labeled contraindication, or hypersensitivity to at least ONE conventional agent prerequisite* AND 2) ONE of the following: a) The patient's medication history indicates use of TWO of the preferred biologic immunomodulator agents (Enbrel, Humira, Simponi, or Stelara) or the patient has a documented intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration), FDA labeled contraindication, or hypersensitivity to TWO of the preferred agents (evidence of a paid claim within the past 999 days, or patient is new to the claim system within the past 120 days and a statement by the physician that patient has taken the preferred agent in the past 999 days) OR b) The patient's diagnosis is indicated in only one of the preferred agents and the patient's medication history indicates use of this preferred medication OR the patient has the documented intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration), FDA labeled contraindication, or hypersensitivity to this preferred agent. OR c) The request is for a FDA labeled indication that is not covered by both of the preferred biologic immunomodulator agents AND 3. The patient does not have any FDA labeled contraindications to therapy with the requested agent AND 4. The patient has been tested for latent TB when required by the prescribing information AND if positive the patient has begun therapy for active TB AND 5. The patient is not currently being treated with another biologic immunomodulator agent AND 6. ONE of the following: a. The prescribed dosage is within the program set limit (FDA approved labeled dosage) OR b. The quantity (dose) requested is greater than the maximum dose recommended in FDA approved labeling, and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist *NOTE: Conventional agent required for diagnoses of rheumatoid arthritis, juvenile idiopathic arthritis, systemic juvenile idiopathic arthritis, psoriatic arthritis, psoriasis, ulcerative colitis, or Crohn's disease Length of approval: □ 12 months for all non-preferred agents except. □ The agents with indications that require loading doses for the new starts listed in Table 2 below. For agents that require a loading dose for a new start, approve the loading dose noted in the table and also the maintenance dose for the remainder of the 12 months." ▪ Removed "Table 2: Non-preferred Agents with indications that require loading doses" ▪ Updated the FDA Labeled Indications for Biologic Immunomodulators and Conventional Agent Prerequisites by Indication charts to add Uveitis indications and prerequisites
	Rationale section updated
	Revision section updated to remove details of the 01-01-2014 update.
	References updated
10-01-2016	In Policy section: ▪ Updated Quantity Limit chart to add Orencia ClickJect.
	References updated
12-01-2016	Policy published 12-29-2016. Policy retro-effective to 12-01-2016.
	In Description section: Updated FDA Approved Indications and Dosage chart to expand indication for Enbrel for treatment of plaque psoriasis in patients 4 years and older.
01-01-2017	Policy published 12-29-2016. Policy effective 01-01-2017.
	In Description section: ▪ Removed Otezla (apremilast) from the policy to be it's own stand-alone policy effective January 1, 2017.

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	▪ FDA Approved Indications and Dosage chart updated to include: Adding to Stelara the indication for treatment of Crohn's Disease, Removing JIA as an indication as PJIA is the more appropriate term for this policy, and Removing reference to infused drugs as they are not pertinent to this policy.
	In Policy section: ▪ In Initial Evaluation Items 1 c ii 1), 1 c v and Renewal Evaluation Item 4 "or Otezla" to read"…another biologic immunomodulator agent or Otezla…" Initial Evaluation ▪ In Item 1 c iv added "The patient has a diagnosis of Crohn's disease" ▪ In *NOTE added "polyarticular" to read "polyarticular juvenile idiopathic arthritis" Renewal Evaluation ▪ In Item 1 added "(*please note Stelara renewal must be for the same strength as the initial approval)" ▪ Updated the following charts: FDA Labeled Indications for Biologic Immunomodulators, Conventional Agent Prerequisites by Indication, Agent Contraindicated as Concomitant Therapy, Contraindication, and Quantity Limits.
	References updated
07-01-2017	Policy published 07-14-2017. Policy retro-effective to 07-01-2017.
	Description section updated ▪ Added Kevzara (sarilumab) as a nonpreferred drug ▪ Updated FDA Approved Indications and Dosage chart to add Kevzara and update Orencia dosage.
	In Policy section ▪ Updated FDA Labeled Indications for Biologic Immunomodulators, Contraindication, and Agent Contraindicated as Concomitant Therapy charts. ▪ Updated Quantity Limits chart to add Kevzara and update Orencia.
	Rationale section updated
	Revision section updated to remove revision details for: 01-01-2014, 06-01-2014, 08-15-2014, 10-01-2014, 04-01-2015, 05-01-2015.
	References updated
10-01-2017	Published 09-01-2017. Effective 10-01-2017.
	In Description Section: ▪ Added Siliq (brodalumab) and Tremfya as nonpreferred Target Drugs ▪ In FDA Approved Indications and Dosage chart added Siliq and Tremfya.
	In Policy Section: ▪ In Length of approval first bullet added "Siliq for plague psoriasis (PS)" to read "12 months for all agents EXCEPT Humira (adalimumab) for ulcerative colitis (UC), Siliq for plaque psoriasis (PS),…" ▪ In Length of approval added third bullet added "Siliq for PS for 16 weeks." ▪ Added Siliq and Tremfya to FDA Labeled Indications for Biologic Immunomodulators, Agents Contraindicated as Concomitant Therapy, Contraindications, and Quantity Limits charts.
	Rationale section updated
	References updated
10-15-2017	Published 09-01-2017. Effective 10-15-2017.
	In Description Section: ▪ In FDA Approved Indications and Dosage chart updated Dosage and Administration for Acterma, Humira, Kineret, and Orencia. ▪ In FDA Approved Indications and Dosage chart added the HS and GIANT CELL ARTERITIS indication and removed the WG/MPA, NHL, CLL, and HC indications.
	In Policy Section: ▪ In Item 1 a added "(starting on samples is not approvable)" to read "There is documentation that the patient is currently being treated with the requested agent (starting on samples is not approvable)" ▪ In Item 1 b added "(starting on samples is not approvable)" to read "The prescriber states the patient is using the requested agent (starting on samples is not approvable) AND is at risk if therapy is changed" ▪ In Item 1 c i added "or an indication supported by drugdex 1 or 2a level of evidence" to read "The patient has an FDA labeled indication or an indication supported by drugdex 1 or 2a level of evidence for the requested agent"

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	▪ In Item 1 c ii 1) added "or an indication supported by drugdex 1 or 2a level of evidence" to read "The patient's medication history indicates use of another biologic immunomodulator agent OR Otezla for the same FDA labeled or an indication supported by drugdex 1 or 2a level of evidence indication" ▪ In "*NOTE" added "or giant cell arteritis" to read "*NOTE: Conventional agent required for diagnoses of rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, systemic juvenile idiopathic arthritis, psoriatic arthritis, psoriasis, Crohn's disease, ulcerative colitis, uveitis, or giant cell arteritis." ▪ In the Conventional Agent Prerequisites by Indication chart added "Giant Cell Arteritis" ▪ In Quantity Limits chart, updated Acterma and Stelara dosage availability.
	Rationale section updated
	References updated
01-01-2018	In Description section: ▪ Revised FDA Approved Indications and Dosage chart format ▪ Added chart to identify Try/Fail criteria for Preferred and Non-preferred drugs by Disease State.
	In Policy section: ▪ In Item 1 c I removed "indication or an indication supported by" and added "indication" to read "The patient has an FDA labeled / drugdex 1 or 2a level of evidence indication for the requested agent" ▪ In Item 1 c ii 1) removed "or an indication supported by" and added "for the requested agent" to read "The patient's medication history indicates use of another biologic immunomodulator agent OR Otezla for the same FDA labeled / drugdex 1 or 2a level of evidence indication for the requested agent" ▪ In Item 1 c iii 1) removed "use of TWO of the preferred biologic immunomodulator agents (Enbrel, Humira, Simponi, or Stelara)" and "TWO of the" and added "trial and failure of the required amount of preferred biologic immunomodulator agents (See preferred Agent Table)" and "all of the required" to read "The patient's medication history indicates trial and failure of the required amount of preferred biologic immunomodulator agents (See preferred Agent Table) or the patient has a documented intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration), FDA labeled contraindication, or hypersensitivity to all of the required" ▪ In Item 1 c iii removed "The patient's diagnosis is indicated in only one of the preferred agents and the patient's medication history indicates use of this preferred medication OR the patient has the documented intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration), FDA labeled contraindication, or hypersensitivity to this preferred agent" ▪ In Item 1 c iii 3) removed "is not covered by two of the" and added "does not require a" to read "The request is for an FDA labeled indication that does not require a preferred product" ▪ Updated the FDA Labeled Indications for Biologic Immunomodulators chart. ▪ Updated the Quantity Limits chart adding Enbrel mini cartridges
	References updated
01-26-2018	In Description section: ▪ Updated FDA Approved Indications and Dosage chart to add new indication for Xeljanz XR and clarify Stelara indication. ▪ Updated Disease State chart to add Xeljanz (XR) to Psoriatic Arthritis disease state.
	In Policy section: ▪ Updated Conventional Agent Prerequisites by Indication and Agents Contraindicated as Concomitant Therapy charts.
	Rationale section updated
05-21-2018	Policy published 05-23-2018. Policy retro-effective to 05-21-2018.
	In Policy section: ▪ Updated Quantity Limit chart to add new Humira agents as targets.
06-15-2018	Description section updated
	Description section updated to match requested indication/diagnosis with any preferred agents/prerequisite requirements
	In Policy section: Initial Evaluation ▪ Added "Preferred and Nonpreferred agents will be approved when the following criteria are met:" ▪ In Item 1 c i added "a. The patient's diagnosis is rheumatoid arthrisis (RA) AND ONE of the following: 1) The patient has had an inadequate response to maximally tolerated methotrexate (e.g., titrated to 25 mg weekly) for at least 3-months OR

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	2) The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to methotrexate OR 3) The patient has had an inadequate response to another conventional agent (e.g., hydroxychloroquine, leflunomide, or sulfasalazine) used in the treatment of RA for at least 3-months OR 4) The patient has a documented intolerance, FDA labeled contraindication or hypersensitivity to another conventional agent for RA OR 5) The patient's medication history indicates use of another biologic immunomodulator agent for RA OR" ▪ In Item 1 c ii 1) added "based on the requested indication", "AND Try and Fail Column" and "for the requested indication" to read "The patient's medication history indicates trial and failure of the required amount of preferred agents based on the requested indication (See Preferred Agent AND Try and Fail Column) OR the patient has a documented intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration), FDA labeled contraindication, or hypersensitivity to ALL of the required preferred agents for the requested indication" ▪ In Item 5 removed "prescribed dosage" and added "quantity (dose) requested" to read "The quantity (dose) requested is within the program limit (FDA approved labeled dosage)" Renewal Evaluation ▪ In Item 5 a removed "prescribed dosage" and added "quantity (dose) requested" to read "The quantity (dose) requested is within the program limit (FDA approved labeled dosage)" ▪ Updated the following charts: FDA Labeled Indications for Biologic Immunomodulators; Conventional Agent Prerequisites by Indication, Contraindication(s); Contraindications
	Rationale section updated
	References updated
06-18-2018	Policy published 07-18-2018. Policy retro-effective to 06-18-2018.
	In Description Section: ▪ Target Agents chart updated adding "Cimzia" as a Non-preferred agents for Psoriatic Arthritis and Zeljanz as a Non-preferred agent for Ulcerative Colitis ▪ FDA Approved Indications and Dosage chart updated adding "PS" to Cimzia and revising the Dosage and Administration for Xeljanz
	In Policy Section: ▪ FDA Labeled Indications for Biologic Immunomodulators chart updated ▪ Contraindications chart updated ▪ Quantity Limits chart updated
	References updated
07-02-2018	Policy published 07-18-2018. Policy retro-effective to 07-02-2018.
	In Description Section ▪ Added "Olumiant" as a Target Agent and to the FDA Approved Indications and Dosage chart
	In Policy section: ▪ Added Olumiant to the FDA Labeled Indications for Biologic Immunomodulators; the Agents Contraindicated as Concomitant Therapy; Contraindications; and the Quantity Limits charts
	References updated
07-16-2018	Policy published 08-15-2018. Policy retro-effective to 07-16-2018.
	In Policy section: Updated Quantity Limits chart with the following: ▪ Added Xeljanz 10mg ▪ Changed QL for Xeljanz 5mg from 4 tabs per day to 2 tabs per day
08-20-2018	Policy published 09-26-2018. Policy retro-effective to 08-20-2018.
	In Policy section: ▪ Quantity Limits chart updated to add new Humira starter kits.
09-01-2018	In Description section Preferred and Nonpreferred Biologic Immunomodulators chart added. Disease State Chart updated FDA Approved Indications and Dosage Chart updated

REVISIONS

In Policy section:

Summary of revisions:

- Update language for prerequisites and preferred to “tried and had an inadequate response”
- Addition of prerequisites and length of therapy trial (to ensure adequate time had elapsed for clinical response/failure) for prerequisites according to clinical practice guidelines
  - o Indications with prerequisites not previously required: ankylosing spondylitis, hidradenitis suppurative
- Require 3 months trial of preferred agents – time frame for clinical response to be consistent
- Addition of specialist or consultation of specialist – to concerns of inappropriate staging/diagnosis and/or starting biologics without assessing for conventional agents first
- Add option if patient is currently being treated with a biologics/Otezla to discontinue prior to starting requested agent
- Enbrel 25 mg/0.5 mL syringe QL decrease to 4 syringes/28 days; dose optimize. Per Enbrel label, to achieve pediatric doses other than 25 mg or 50 mg, use reconstituted Enbrel lyophilized powder
- QL update to match how supplied (mL, pens, syringe, etc)
  - o Update Kineret to match others – per 28 days (instead of 30 days)
- Clarify for the diagnosis of RA – prerequisites should also be used in treatment of RA or previous biologics use must be FDA approved for RA
- Addition of option to accept preferred agent
- Renewal – for concomitant biologic use, change “starting” to “continuing” since patients would have already started the requested agent
- Reduce QL for Xeljanz 5mg from 4 tablets daily to 2 tablets daily to dose optimize since Xeljanz 10 mg is not available
- Administrative additions:
  - o Olumiant – QL 1 tablet daily, Xeljanz 10 mg – QL 2 tablets daily

Initial Evaluation

▪ In header, removed "Preferred and Nonpreferred" and added "Targeted" to read "Targeted agents will be approved when the following are met:"
▪ In 1 C i a added "that is labeled for the requested agent" to read "The patient has a diagnosis of rheumatoid arthritis (RA) that is labeled for the requested agent AND ONE of the following:"
▪ In 1 C i a 1) and 1 C i a 3) added "tried and" to read " The patient has tried and had an inadequate response to..."
▪ In 1 C i b added "and route of administration" to read "The patient has an FDA labeled indication or an indication supported in DrugDex with 1 or 2a level of evidence (or otherwise accepted by client) for the requested agent and route of administration..."
▪ In 1 C i b added "1) The patient has tried and had an inadequate response to ONE conventional agent for the required length of therapy*"
▪ In 1 C ii added "1) The requested agent is a preferred agent for the requested indication OR
2) The requested indication does NOT require any preferred agents"
▪ In 1 C ii 3) added "has tried and had an inadequate response to", and "for at least 3 months", and removed "medication history indicates trial and failure of" to read "The patient has tried and had an inadequate response to the required amount of preferred agents for the requested indication for at least 3 months (See Preferred Agent AND Try and Fail Column)"
▪ In 1 C ii removed "The request is for an FDA labeled indication that does NOT require a preferred agent"
▪ In 1 C iii) added "tried and" and removed "failed" and "a trial of" to read "...the patient has tried and had an inadequate response to Stelara 45mg for at least 3 months"
▪ In Item 2 added "The prescriber is a specialist in the area of the patient’s requested indication or has consulted with a specialist in the area of the patient’s requested indication (e.g. rheumatologist for JIA, PsA, RA; gastroenterologist for CD, UC; dermatologist for PS; oncologist for CRS)"
▪ In Item 3 B added "The patient is currently being treated with another biologic immunomodulator agent or Otezla AND will discontinue prior to starting the requested agent"
▪ In Item 5 removed "active" and added "latent" to read "... if positive the patient has begun therapy for latent TB"
▪ In Item 6 A removed "FDA approved labeled dosage" and added "quantity" to read "The quantity (dose) requested is within the program quantity limit"

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	In Item 6 B removed "maximum dose recommended in FDA approved labeling" and added "program quantity limit" to read "The quantity (dose) requested is greater than the program quantity limit…" ▪ In the *Note added "ankylosing spondylitis" and "hidradenitis suppurative" to read "*NOTE: Conventional agent required for diagnoses of ankylosing spondylitis, Crohn's disease, giant cell arteritis, hidradenitis suppurative, polyarticular juvenile idiopathic arthritis, psoriatic arthritis, psoriasis, rheumatoid arthritis, systemic juvenile idiopathic arthritis, ulcerative colitis, and uveitis." ▪ In Length of Approval added "Xeljanz for UC may be approved for 16 weeks." ▪ Added "**NOTE: Cosentyx for the diagnoses of AS and PSA loading doses are not approvable." Renewal Evaluation ▪ In header, removed "Preferred and Nonpreferred" and added "Targeted" to read "Targeted agents will be approved when the following are met:" ▪ In Item 2 added "with the requested agent" to read "The patient has shown clinical improvement with the requested agent (i.e. slowing of disease progression or decrease in symptom severity and/or frequency)" ▪ Added 3 "The prescriber is a specialist in the area of the patient's requested indication or has consulted with a specialist in the area of the patient's requested indication (e.g. rheumatologist for JIA, PsA, RA; gastroenterologist for CD, UC; dermatologist for PS; oncologist for CRS)" ▪ In Item 4 added "The patient is currently being treated with another biologic immunomodulator or Otezla AND will discontinue prior to continuing the requested agent" ▪ In Item 7 A removed "FDA approved labeled dosage" and added "quantity" to read "The quantity (dose) requested is within the program quantity limit" ▪ In Item 7 B removed "maximum dose recommended in FDA approved labeling" and added "program quantity limit" to read "The quantity (dose) requested is greater than the program quantity limit AND the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist" ▪ Removed FDA Labeled Indications for Biologic Immunomodulators chart and the Conventional Agent Prerequisites by Indication chart and added the Indication / Conventional Agent Prerequisites / Trial Length chart ▪ Updated the Quantity Limits chart
	Rationale section updated
	References updated
09-01-2018	Policy published 1012-2018. Policy effective 09-01-2018
	In Quantity Limit Chart Stelara quantity limit corrected.

REFERENCES

1. Humira prescribing information. AbbVie, Inc. December 2017.
2. Enbrel prescribing information. Immunex Corporation. May 2018.
3. Remicade prescribing information. Janssen Biotech, Inc. October 2017.
4. Cimzia prescribing information. UCB, Inc. May 2018.
5. Siliq prescribing information. Valeant Pharmaceuticals. February 2017.
6. Orencia prescribing information. E.R. Squibb & Sons. June 2017.
7. Tremfya prescribing information. Janssen Biotech, Inc. October 2017.
8. Simponi prescribing information. Janssen Biotech, Inc. March 2018.
9. Stelara prescribing information. Janssen Biotech, Inc. February 2018.
10. Renflexis prescribing information. Merck Sharp & Dohme Corp. April 2017.
11. Actemra prescribing information. Genentech, Inc. May 2018.
12. Taltz prescribing information. Eli Lilly and Company. April 2018.
13. Entyvio prescribing information. Takeda Pharmaceuticals America, Inc. February 2018
14. Cosentyx Prescribing Information. Novartis Pharmaceuticals Corp. January 2018.
15. Xeljanz and Xeljanz XR prescribing information. Pfizer, Inc. May 2018.
16. Simponi ARIA prescribing information. Jansen Biotech, Inc. February 2018.
17. Inflectra prescribing information. Celltrion, Inc. December 2017.

18. Kevzara prescribing information. Regeneron Pharmaceuticals, Inc/ Sanofi-Aventis U.S. LLC. May 2017.
19. Kineret prescribing information. Swedish Orphan Biovitrum. June 2018.
20. Yu, David, MD, et al. Assessment and Treatment of Ankylosing Spondylitis in Adults. UpToDate. Last updated April 2016. Literature review through March 2018.
21. Ward, Michael M, MD, MPH, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Rheumatol. 2016 February; 68(2): 282–298.
22. Moreland, Larry W., MD., et al. General Principles of Management of Rheumatoid Arthritis in Adults. UpToDate. Last updated July 2016. Literature review through February 2018.
23. Jasvinder A. Singh, Saag, K, et al. 2015 American College of Rheumatology Guideline for the treatment of Rheumatoid Arthritis*. Arthritis Care and Research*. 2015.
24. Cohan, Stanley, MD., et al. Initial Treatment of Rheumatoid Arthritis in Adults. UpToDate. Last Updated January 2018.
25. Cohan, Stanley, MD., et al. Treatment of Rheumatoid Arthritis in Adults Resistant to Initial Nonbiologic DMARD Therapy. UpToDate. Last updated September 2017. Literature review through February 2018.
26. Weiss, Pamela, MD, MSCE, et al. Polyarticular Juvenile Idiopathic Arthritis: Treatment. UpToDate. Last Updated November 2017. Literature current through February 2018.
27. Kimura, Yukiko, MD, et al. Systemic Juvenile Idiopathic Arthritis: Treatment. UpToDate. Last updated August 2016. Literature review through February 2018.
28. Ringold, Sarah, et al. 2013 Update of the 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis. American College of Rheumatology. October 2013. *Arthritis & Rheumatism*. Vol 65 (10): 2499-2512.
29. Gladman, Dafna D., MD, FRCPC, et al. Treatment of Psoriatic Arthritis. UpToDate. Last updated February 2018.
30. Weigle, Nancy, MD, et al. Psoriasis. American Academy of Family Physicians. May 2013. 87 (9): 626-633.
31. Feldman, Steven R, MD, PhD, et al. Treatment of Psoriasis in Adults. UpToDate. Last updated November 2017. Literature review through February 2018.
32. Ingram, John R., MD, PhD., et al. Hidradenitis Suppurativa: Treatment. UpToDate. Last updated April 2018.
33. Terdiman, Jonathan P., et al. American Gastroenterological Association Institute Guideline on the Use of Thiopurines, Methotrexate, and Anti-TNF-α Biologics Drugs for the Induction and Maintenance of Remission in Inflammatory Crohn's Disease. *Gastroenterology* 2013; 145: 1459-1463.
34. MacDermott, Richard P., MD, et al. Management of Mild to Moderate Ulcerative Colitis in Adults. UpToDate. Last updated August 2017. Literature review through March 2018.
35. Peppercorn, Mark A., et al. Management of Severe Ulcerative Colitis in Adults. UpToDate. Last updated March 2018.
36. Cohen, Russell D., MD, FACG, AGAF., et al. Approach to Adults with Steroid-Refractory and Steroid-Dependent Ulcerative Colitis. UpToDate. Last updated November 2017. Literature review through March 2018.
37. Rosenbaum, James T., MD, et al. Uvetitis: Etiology, Clinical Manifestation, and Diagnosis. UpToDate. Last updated February 2017. Literature review through March 2018.
38. Rosenbaum, James T., MD, et al. Uveitis: Treatment. UpToDate. Last updated August 2017. Literature review through March 2018.
39. Docken, William P., MD., et al. Treatment of Giant Cell Arteritis. UpToDate. Last updated March 2018.
40. American College of Rheumatology. Cryopyrin-Associated Autoinflammatory Syndromes. Updated March 2017. Available at: https://www.rheumatology.org/I-Am-A/Patient-Caregiver/Diseases-Conditions/Cryopyrin-Associated-Autoinflammatory-Syndrome-CAPS-Juvenile. Accessed 4/10/18

41. Nigrovic, Peter A., MD., et al. Cryopyrin-Associated Periodic Syndromes and Related Disorders. UpToDate. Last updated June 2017. Literature review through March 2018.
42. Olumiant prescribing information. Eli Lilly and Company. May 2018.