Clinical Policy Title:	Biologic DMARDs
Policy Number:	RxA.592
Drug(s) Applied:	Actemra®, Cimzia®, Cosentyx®, Enbrel®, Entyvio®, Humira®, Ilumya™, Inflectra®, Kevzara®, Kineret®, Olumiant®, Orencia®, Otezla®, Remicade®, Renflexis™, Rinvoq™, Siliq™, Simponi®, Simponi Aria®, Skyrizi™, Stelara®, Taltz®, Tremfya®, Tysabri®, Xeljanz®, Xeljanz® XR, Xeljanz® oral Solution
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

The following are biologic disease-modifying anti-rheumatic drugs (DMARDs) requiring prior authorization: tocilizumab (Actemra®), certolizumab pegol (Cimzia®), secukinumab (Cosentyx®), etanercept (Enbrel®), vedolizumab (Entyvio®), adalimumab (Humira®), tildrakizumab-asmn (Ilumya™), infliximab-dyyb (Inflectra®), sarilumab (Kevzara®), anakinra (Kineret®), baricitinib (Olumiant®), abatacept (Orencia®), apremilast (Otezla®), infliximab (Remicade®), infliximab-abda (Renflexis™), upadacitinib (Rinvoq™), brodalumab (Siliq™), golimumab (Simponi®, Simponi Aria®), risankizumab-rzaa (Skyrizi™), ustekinumab (Stelara®), ixekizumab (Taltz®), guselkumab (Tremfya®), natalizumab (Tysabri®), tofacitinib (Xeljanz®, Xeljanz® XR, Xeljanz® oral Solution).

	AS	nr axSpA	CD	UC	GCA	NOMID	PJIA	SJIA	PsO	PsA	RA	HS	MS	UV	CRS	BD
Actemra®					x		x[#]	x[#]			x[#]				x*	
Cimzia®	x	x	x						x	x	x					
Cosentyx®	x	x							x	x						
Enbrel®	x						x		x	x	x					
Entyvio®			x	x												
Humira®	x		x	x			x		x	x	x	x		x		
Ilumya™									x							
Inflectra®	x		x	x					x	x	x					
Kevzara®											x					
Kineret®						x					x					

	AS	nr axSpA	CD	UC	GCA	NOMID	PJIA	SJIA	PsO	PsA	RA	HS	MS	UV	CRS	BD
Olumiant®											x					
Orencia®							x			x	x					
Otezla®									x	x						x
Remicade®	x		x	x					x	x	x					
Renflexis™	x		x	x					x	x	x					
Rinvoq™											x					
Siliq™									x							
Simponi®	x			x						x	x					
Simponi Aria®	x						x			x	x					
Skyrizi™									x							
Stelara®			x[#]	x					x	x						
Taltz®	x	x							x	x						
Tremfya®									x	x						
Tysabri®			x										x			
Xeljanz®/ Xeljanz® XR				x			x			x	x					

* =IV only; # =IV/SC; ^ = SC only

AS=ankylosing spondylitis; nr-axSpA=non-radiographic axial spondyloarthritis; CD=Crohn's disease; UC=ulcerative colitis; GCA = giant cell arteritis; NOMID=neonatal-onset multisystem inflammatory disease; PJIA=polyarticular juvenile idiopathic arthritis; SJIA=systemic juvenile idiopathic arthritis; PsO=plaque psoriasis; PsA=psoriatic arthritis; RA=rheumatoid arthritis; HS=hidradenitis suppurativa, MS=multiple sclerosis, UV=uveitis; CRS=cytokine release syndrome; BD=Behçet's disease.

Dosing Information			
Dosing Regimen	**Maximum Dose**	**Dosing Regimen**	**Maximum Dose**
abatacept (Orencia®)	RA PsA	IV: weight-based dose at weeks 0, 2, and 4, followed by every 4 weeks Weight < 60 kg: 500 mg per dose Weight 60 to 100 kg: 750 mg per dose Weight > 100 kg: 1,000 mg per dose SC: 125 mg once weekly (For RA: if single IV loading dose is given, start first SC injection within one day of IV dose)	IV: 1,000 mg every 4 weeks SC: 125 mg/week
	PJIA	IV: weight-based dose at weeks 0, 2, and 4, followed by every 4 weeks Weight < 75 kg: 10 mg/kg per dose Weight 75 to 100 kg: 750 mg per dose Weight >100 kg: 1,000 mg per dose	IV: 1,000 mg every 4 weeks SC: 125 mg/week
		SC: weight-based dose once weekly Weight 10 to < 25 kg: 50 mg per dose Weight 25 to < 50 kg: 87.5 mg per dose Weight ≥ 50 kg: 125 mg per dose	
adalimumab (Humira®)	RA	40 mg SC every other week Some patients with RA not receiving concomitant methotrexate may benefit from increasing the frequency to 40 mg every week.	40 mg/week
	PJIA	Weight 10 kg (22 lbs) to < 15 kg (33 lbs): 10 mg SC every other week Weight 15 kg (33 lbs) to < 30 kg (66 lbs): 20 mg SC every other week Weight ≥ 30 kg (66 lbs): 40 mg SC every other week	40 mg every other week
	PsA AS	40 mg SC every other week	40 mg every other week
	CD	Initial dose: **Adults:** 160 mg SC on Day 1, then 80 mg SC on Day 15 **Pediatrics:** Weight 17 kg (37 lbs) to < 40 kg (88 lbs): 80 mg SC on Day 1, then 40 mg SC on Day 15 Weight ≥ 40 kg (88 lbs): 160 mg SC on Day 1, then 80 mg SC on Day 15	40 mg every other week

		Maintenance dose: **Adults:** 40 mg SC every other week starting on Day 29 **Pediatrics*:*** Weight 17 kg (37 lbs) to < 40 kg (88 lbs): 20 mg SC every other week starting on Day 29 Weight ≥ 40 kg (88 lbs): 40 mg SC every other week starting on Day 29	
	UC	Initial dose: 160 mg SC on Day 1, then 80 mg SC on Day 15 Maintenance dose: 40 mg SC every other week starting on Day 29	40 mg every other week
	PsO	Initial dose: 80 mg Maintenance dose: 40 mg SC every other week starting one week after initial dose	40 mg every other week
	UV	Pediatrics: Weight 10 kg (22 lbs) to < 15 kg (33 lbs): 10 mg SC every other week Weight 15 kg (33 lbs) to < 30 kg (66 lbs): 20 mg SC every other week Weight ≥ 30 kg (66 lbs): 40 mg SC every other week	40 mg every other week
	HS	Adults: For patients 12 years of age and older weighing at least 30 kg: Initial dose: Weight 30 kg (66 lbS) to < 60 kg (132 lbs): 80 mg SC on Day 1, then 40 mg on Day 8 Weight ≥ 60 kg (132 lbs): 160 mg SC on Day 1, then 80 mg SC on Day 15 Maintenance dose: Weight 30 kg (66 lbS) to < 60 kg (132 lbs): 40 mg every other week Weight ≥ 60 kg (132 lbs): 40 mg SC once weekly starting on Day 29	40 mg/week
anakinra (Kineret®)	RA	100 mg SC once daily	100 mg/day
	NOMID	Initial dose: 1 – 2 mg/kg SC once daily or divided BID Maintenance dose: 8 mg/kg SC once daily or divided BID	8 mg/kg/day
apremilast (Otezla®)	PsO PsA BD	Initial dose: Day 1: 10 mg PO QAM Day 2: 10 mg PO QAM and 10 mg PO QPM Day 3: 10 mg PO QAM and 20 mg PO QPM	60 mg/day

		Day 4: 20 mg PO QAM and 20 mg PO QPM Day 5: 20 mg PO QAM and 30 mg PO QPM Maintenance dose: Day 6 and thereafter: 30 mg PO BID	
baricitinib (Olumiant™)	RA	2 mg PO once daily	2 mg/day
brodalumab (Siliq™)	PsO	Initial dose: 210 mg SC at weeks 0, 1, and 2 Maintenance dose: 210 mg SC every 2 weeks	210 mg every 2 weeks
certolizumab (Cimzia®)	CD	Initial dose: 400 mg SC at 0, 2, and 4 weeks Maintenance dose: 400 mg SC every 4 weeks	400 mg every 4 weeks
	RA PsA AS nr-axSpA	Initial dose: 400 mg SC at 0, 2, and 4 weeks Maintenance dose: 200 mg SC every other week (or 400 mg SC every 4 weeks)	400 mg every 4 weeks
	PsO	400 mg SC every other week. For some patients (with body weight ≤ 90 kg), a dose of 400 mg SC at 0, 2 and 4 weeks, followed by 200 mg SC every other week may be considered.	400 mg every other week
etanercept (Enbrel®)	RA PsA	25 mg SC twice weekly or 50 mg SC once weekly	50 mg/week
	AS	50 mg SC once weekly	50 mg/week
	PJIA	Weight < 63 kg: 0.8 mg/kg SC once weekly Weight ≥ 63 kg: 50 mg SC once weekly	50 mg/week
	PsO	Adults: Initial dose: 50 mg SC twice weekly for 3 months Maintenance dose: 50 mg SC once weekly Pediatrics: Weight < 63 kg: 0.8 mg/kg SC once weekly Weight ≥ 63 kg: 50 mg SC once weekly	50 mg/week
golimumab (Simponi®)	AS PsA RA	50 mg SC once monthly	50 mg/month
	UC	Initial dose: 200 mg SC at week 0, then 100 mg SC at week 2 Maintenance dose: 100 mg SC every 4 weeks	100 mg every 4 weeks
golimumab (Simponi Aria®)	AS PsA RA	Initial dose: 2 mg/kg IV at weeks 0 and 4 Maintenance dose: 2 mg/kg IV every 8 weeks	2 mg/kg every 8 weeks
	PJIA	Initial dose: 80 mg/m^2 at weeks 0 and 4 Maintenance dose: 2 mg/kg IV every 8 weeks	80 mg/m^2 every 8 weeks
guselkumab	PsO, PsA	Initial dose: 100 mg SC at weeks 0 and 4	100 mg

(Tremfya®)		Maintenance dose: 100 mg SC every 8 weeks	every 8 weeks
infliximab (Remicade®, Renflexis™, Inflectra®)	CD, UC	Initial dose: 5 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: 5 mg/kg IV every 8 weeks. For CD: Some adult patients who initially respond to treatment may benefit from increasing the dose to 10 mg/kg if they later lose their response.	CD, Adults: 10 mg/kg every 8 weeks UC, Adults: 5 mg/kg every 8 weeks Pediatrics: 5 mg/kg every 8 weeks
	PsA PsO	Initial dose: 5 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: 5 mg/kg IV every 8 weeks	5 mg/kg every 8 weeks
infliximab (Remicade®, Renflexis™, Inflectra®)	RA	In conjunction with MTX Initial dose: 3 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: 3 mg/kg IV every 8 weeks Some patients may benefit from increasing the dose up to 10 mg/kg or treating as often as every 4 weeks	10 mg/kg every 4 weeks
	AS	Initial dose: 5 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: 5 mg/kg IV every 6 weeks	5 mg/kg every 6 weeks
ixekizumab (Taltz®)	PsO (with or without coexistent PsA)	Initial dose: 160 mg (two 80 mg injections) SC at week 0, then 80 mg SC at weeks 2, 4, 6, 8, 10, and 12 Maintenance dose: 80 mg SC every 4 weeks	80 mg every 4 weeks
	PsA ,AS	Initial dose: 160 mg (two 80 mg injections) SC Maintenance dose: 80 mg SC every 4 weeks	80 mg every 4 weeks
	nraxSpA	80 mg SC every 4 weeks	80 mg every 4 weeks
natalizumab (Tysabri®)	MS, CD	300 mg IV every 4 weeks	300 mg every weeks
Risankizumab-rzaa (Skyrizi®)	PsO	150 mg SC at weeks 0, 4, and every 12 weeks thereafter	150 mg/12 weeks
sarilumab (Kevzara®)	RA	200 mg SC once every two weeks	200 mg/2 weeks
secukinumab (Cosentyx®)	PsO (with or without PsA)	300 mg SC at weeks 0, 1, 2, 3, and 4, followed by 300 mg SC every 4 weeks. (for some patients, a dose of 150 mg may be acceptable)	300 mg every 4 weeks
	PsA	With loading dose: 150 mg SC at week 0, 1, 2, 3, and 4, followed by 150 mg SC every 4 weeks Without loading dose: 150 mg SC every 4 weeks If a patient continues to have active psoriatic	300 mg every 4 weeks

		arthritis, consider a dosage of 300 mg.	
secukinumab (Cosentyx®)	AS nr-axSpA	With loading dose: 150 mg SC at weeks 0, 1, 2, 3, and 4, followed by 150 mg SC every 4 weeks thereafter Without loading dose: 150 mg SC every 4 weeks	150 mg every 4 weeks
tildrakizumab-asmn (Ilumya™)	PsO	Initial dose: 100 mg SC at weeks 0 and 4 Maintenance dose: 100 mg SC every 12 weeks Tildrakizumab should only be administered by a healthcare professional.	100 mg every 12 weeks
tocilizumab (Actemra®)	RA	IV: 4 mg/kg every 4 weeks followed by an increase to 8 mg/kg every 4 weeks based on clinical response SC: Weight < 100 kg: 162 mg SC every other week, followed by an increase to every week based on clinical response Weight ≥ 100 kg: 162 mg SC every week	IV: 800 mg every 4 weeks SC: 162 mg every week
	GCA	162 mg SC every week (every other week may be given based on clinical considerations)	SC: 162 mg every week
	PJIA	Weight < 30 kg: 10 mg/kg IV every 4 weeks or 162 mg SC every 3 weeks Weight ≥ 30 kg: 8 mg/kg IV every 4 weeks or 162 mg SC every 2 weeks	IV: 10 mg/kg every 4 weeks SC: 162 mg every 2 weeks
	SJIA	IV: Weight < 30 kg: 12 mg/kg IV every 2 weeks Weight ≥ 30 kg: 8 mg/kg IV every 2 weeks SC: Weight < 30 kg: 162 mg SC every 2 weeks Weight ≥ 30 kg: 162 mg SC every week	IV: 12 mg/kg every 2 weeks SC: 162 mg every week
	CRS	Weight < 30 kg: 12 mg/kg IV per infusion Weight ≥ 30 kg: 8 mg/kg IV per infusionn If no clinical improvement in the signs and symptoms of CRS occurs after the first dose, up to 3 additional doses of Actemra® may be administered. The interval between consecutive doses should be at least 8 hours.	IV: 800 mg/infusion, up to 4 doses
tofacitinib (Xeljanz®)	PsA RA	5 mg PO BID	10 mg/day

	UC	10 mg PO BID for at least 8 weeks, then 5 or 10 mg BID thereafter. Discontinue after 16 weeks of 10 mg BID if adequate therapeutic benefit is not achieved.	20 mg/day
tofacitinib (Xeljanz® / Xeljanz® oral Solution)	PJIA	5 mg twice daily or weight-based equivalent twice daily: • 10 kg ≤ body weight <20 kg: 3.2 mg (3.2 mL oral solution) twice daily • 20 kg ≤ body weight <40 kg: 4 mg (4 mL oral solution) twice daily • Body weight ≥40 kg: 5 mg (one 5 mg tablet or 5 mL oral solution) twice daily	5 mg or 5 ml twice daily
tofacitinib extended-release (Xeljanz® XR)	PsA RA	11 mg PO once daily	11 mg/day
upadacitinib (Rinvoq™)	RA	15 mg PO once daily	15 mg/day
ustekinumab (Stelara®)	PsO	Weight based dosing SC at weeks 0 and 4, followed by maintenance dose every 12 weeks Adult: Weight ≤ 100 kg: 45 mg Weight > 100 kg: 90 mg Pediatrics (Age 12 years and older): Weight < 60 kg: 0.75 mg/kg Weight 60 to 100 kg: 45 mg Weight > 100kg: 90 mg	90 mg every 12 weeks
	PsA	45 mg SC at weeks 0 and 4, followed by 45 mg every 12 weeks	45 mg every 12 weeks
	PsA (with co-existent PsO)	Weight > 100 kg: 90 mg SC at weeks 0 and 4, followed by 90 mg every 12 weeks	90 mg every 12 weeks
	CD	Weight based dosing IV at initial dose, followed by 90 mg SC every 8 weeks Weight ≤ 55 kg: 260 mg Weight 55 kg to 85 kg: 390 mg Weight > 85 kg: 520 mg	90 mg every 8 weeks
	CD UC	Initial dose: 300 mg IV at weeks 0, 2, and 6 Maintenance dose: 300 mg IV every 8 weeks	300 mg every 8 weeks

Dosage Forms

- abatacept (Orencia®):
  - Single-use vial: 250 mg
  - Single-dose prefilled syringe: 50 mg/0.4 mL, 87.5 mg/0.7 mL, 125 mg/mL
  - Single-dose prefilled ClickJect™ autoinjector: 125 mg/mL
- adalimumab (Humira®):
  - Single-dose prefilled pen: 80 mg/0.8 mL, 40 mg/0.8 mL, 40 mg/0.4 mL
  - Single-dose prefilled syringe: 80 mg/0.8 mL, 40 mg/0.8 mL, 40 mg/0.4 mL, 20 mg/0.4 mL, 20 mg/0.2 mL, 10 mg/0.2 mL, 10 mg/0.1 mL
  - Single-use vial for institutional use only: 40 mg/0.8 mL
- anakinra (Kineret®): Single-use prefilled syringe: 100 mg/0.67 mL
- apremilast (Otezla®): Tablets: 10 mg, 20 mg, 30 mg
- baricitinib (Olumiant®): Tablets: 1mg, 2 mg
- brodalumab (Siliq™): Single-dose prefilled syringe: 210 mg/1.5 mL
- certolizumab pegol (Cimzia®):
  - Lyophilized powder in a single-use vial for reconstitution: 200 mg
  - Single-use prefilled syringe: 200 mg/mL
- etanercept (Enbrel®):
  - Single-dose prefilled syringe**:** 25 mg/0.5 mL, 50 mg/mL
  - Single-dose prefilled SureClick® Autoinjector: 50 mg/mL Multi-dose vial: 25 mg
  - Enbrel MiniTM single-dose prefilled cartridge for use with AutoTouchTM reusable autoinjector: 50 mg/mL
- golimumab (Simponi®):
  - Single-dose prefilled SmartJect® autoinjector**:** 50 mg/0.5 mL, 100 mg/1 mL
  - Single-dose prefilled syringe: 50 mg/0.5 mL, 100 mg/1 mL
- golimumab (Simponi Aria®): Single-use vial: 50 mg/4 mL
- infliximab-dyyb (Inflectra®): Single-use vial: 100 mg/20 mL
- infliximab (Remicade®): Single-use vial: 100 mg/20 mL
- infliximab-abda (Renflexis™): Single-use vial: 100 mg/20 mL
- ixekizumab (Taltz®):
  - Single-dose prefilled autoinjector: 80 mg/mL
  - Single-dose prefilled syringe: 80 mg/mL
- guselkumab (Tremfya®): Single-dose prefilled syringe**:** 100 mg/mL
- natalizumab (Tysabri®): Single-use vial: 300 mg/15 mL
- risankizumab-rzaa (Skyrizi™): Single-dose prefilled syringe: 75 mg/0.83 mL
- sarilumab (Kevzara®): Single-dose prefilled syringe: 150 mg/1.14 mL, 200 mg/1.14 mL
- secukinumab (Cosentyx®):
  - Single-dose Sensoready® pen**:** 150 mg/mL
  - Single-dose prefilled syringe: 150 mg/mL
  - Single-use vial: 150 mg
- tildrakizumab-asmn (Ilumya™): Single-dose prefilled syringe**:** 100 mg/1 mL
- tocilizumab (Actemra®):
  - Single-use vial**:** 80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL
  - Single-dose prefilled syringe: 162 mg/0.9 mL
  - Single-dose prefilled autoinjector: 162 mg/0.9 mL

- tofacitinib (Xeljanz®):
  - Oral Solution: 1 mg/mL tofacitinib
  - Tablets: 5 mg, 10 mg
- tofacitinib extended-release (Xeljanz® XR): Tablets**:** 11 mg, 22 mg
- upadacitinib (Rinvoq™): Tablets, extended-release**:** 15 mg
- ustekinumab (Stelara®):
  - Single-use prefilled syringe**:** 45 mg/0.5 mL, 90 mg/mL
  - Single-dose vial for SC: 45 mg/0.5 mL
  - Single-dose vial for IV: 130 mg/26 mL (5 mg/mL)
- Vedolizumab (Entyvio®): Single-use vial**:** 300 mg/20 mL

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Axial Spondylitis (must meet all):

1. Diagnosis of active ankylosing spondylitis (AS) or non-radiographic axial spondyloarthritis (nr-axSpA);
2. Request is for one of the following: Humira®, Cimzia®, Cosentyx®, Enbrel®, Inflectra®, Remicade®, Renflexis™, Simponi®, Simponi Aria® or Taltz®;
3. Prescribed by or in consultation with a rheumatologist;
4. Age 18 years of age or older;
5. Failure of at least two (2) non-steroidal anti-inflammatory drugs (NSAIDs) at up to maximally indicated doses, each used for at ≥ 4 weeks unless contraindicated or clinically significant adverse effects are experienced;
6. For Cosentyx®, Enbrel®, or Remicade®: Failure of two (2) of the following: Humira®, Cimzia®, Inflectra®, Renflexis™, Simponi®, Simponi Aria® and Taltz®; each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed maximum dose indicated in background.

Approval duration
Commercial: 12 months
Medicaid: 12 months

B. Behçet's Disease (must meet all)**:**

1. Diagnosis of oral ulcers in members with BD;
2. Request is for Otezla®;
3. Prescribed by or in consultation with a dermatologist or rheumatologist;
4. Age 18 years of age and older;
5. Failure of a topical corticosteroid (e.g., triamcinolone acetonide cream) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Failure of an oral corticosteroid (e.g., prednisone) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
7. Failure of colchicine at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
8. Dose does not exceed 60 mg per day.

Approval duration

Commercial: 12 months
Medicaid: 12 months

C. Crohn's Disease (must meet all)**:**

1. Diagnosis of CD;
2. Request is for one of the following: Humira®, Entyvio®, Cimzia®, Inflectra®, Remicade®, Renflexis™, Stelara®, Tysabri®;
3. Prescribed by or in consultation with a gastroenterologist;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of at least one immunomodulator (e.g., azathioprine, 6-mercaptopurine [6-MP], methotrexate [MTX]) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. Medical justification supports inability to use immunomodulators (see Appendix D);
5. Member meets one of the following (a or b):
   a. For Humira®, Inflectra®, Remicade®, Renflexis®: age 6 years of age or older;
   b. For Cimzia®, Entyvio®, Stelara®, Tysabri®: age 18 years of age or older;
6. For Entyvio®, Remicade®, or Tysabri®: Failure of two (2) of the following for ≥ 3 consecutive months: Humira®, Cimzia®, Inflectra®, Renflexis™, Stelara®, unless contraindicated or clinically significant adverse effects are experienced;
7. For Tysabri®: Not prescribed concurrently with immunosuppressants (e.g., azathioprine, cyclosporine, 6-MP, MTX) or TNF-α inhibitors (note: aminosalicylates may be continued);
8. Dose does not exceed maximum dose indicated in background.

Approval duration
Commercial: 12 months
Medicaid: 12 months

D. Cytokine Release Syndrome (must meet all)**:**

1. Member has a scheduled chimeric antigen receptor (CAR) T-cell therapy (e.g., Kymriah™, Yescarta™);
2. Request is for an intravenous formulation of Actemra®;
3. Dose does not exceed 800 mg per infusion for up to 4 total doses.

Approval duration
Commercial: Up to 4 total doses
Medicaid: Up to 4 total doses

E. Giant Cell Arteritis (must meet all)**:**

1. Diagnosis of GCA;
2. Request is for subcutaneous formulation of Actemra®;
3. Prescribed by or in consultation with a rheumatologist;
4. Age 18 years of age or older;
5. Failure of a trial of ≥ 3 consecutive months of a systemic corticosteroid at up to maximally tolerated doses in conjunction with MTX or azathioprine, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 162 mg SC every week.

Approval duration
Commercial: 12 months
Medicaid: 12 months

F. Hidradenitis Suppurativa (must meet all)**:**

1. Diagnosis of HS;
2. Request is for Humira®;
3. Prescribed by or in consultation with a dermatologist, rheumatologist, or gastroenterologist;
4. Age 12 years of age or older;
5. Documentation of Hurley stage II or stage III (see Appendix D);
6. Failure of a trial of ≥ 3 consecutive months of systemic antibiotic therapy (e.g., clindamycin, minocycline, doxycycline, rifampin) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed maximum dose indicated in background.

Approval duration
Commercial: 12 months
Medicaid: 12 months

G. Neonatal-Onset Multisystem Inflammatory Disease (must meet all)**:**

1. Diagnosis of NOMID or chronic infantile neurological, cutaneous and articular syndrome (CINCA);
2. Request is for Kineret®;
3. Prescribed by or in consultation with a rheumatologist;
4. Dose does not exceed maximum dose indicated in background.

Approval duration
Commercial: 12 months
Medicaid: 12 months

H. Plaque Psoriasis (must meet all)**:**

1. Diagnosis of PsO;
2. Request is for one of the following: Humira®, Cimzia®, Cosentyx®, Enbrel®, Ilumya™, Inflectra®, Otezla®, Remicade®, Renflexis™, Siliq™, Skyrizi™, Stelara®, Taltz® or Tremfya®;
3. Prescribed by or in consultation with a dermatologist or rheumatologist;
4. Member meets one of the following (a or b):
   a. For Humira®, Cimzia®, Cosentyx®, Ilumya™, Inflectra®, Otezla®, Remicade®, Renflexis™, Siliq™, Skyrizi™, Tremfya®: age 18 years of age or older;
   b. For Stelara®, Taltz®: age 6 years of age or older;
   c. For Enbrel®: age 4 years of age or older;
5. Member meets one of the following (a or b):
   a. Failure of a trial of ≥ 3 consecutive months of MTX at up to maximally indicated doses;
   b. Member has intolerance or contraindication to MTX (see Appendix D), and failure of a trial of ≥ 3 consecutive months of cyclosporine or acitretin at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. For Cosentyx®, Enbrel®, Ilumya™, Remicade®, Siliq™ or Tremfya®: Failure of two of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Cimzia®, Humira®, Inflectra®, Otezla®, Renflexis™, Skyrizi™, Stelara®, Taltz®;
7. Dose does not exceed maximum dose indicated in background.

Approval duration
Commercial: 12 months
Medicaid: 12 months

I. Polyarticular Juvenile Idiopathic Arthritis (must meet all)**:**

1. Diagnosis of PJIA;
2. Request is for one of the following: Humira®, Actemra®, Enbrel®, Orencia®, Simponi Aria®, or Xeljanz®/ Xeljanz XR®;
3. Prescribed by or in consultation with a rheumatologist;
4. Age 2 years of age or older;
5. Failure of a trial of ≥ 3 consecutive months of MTX at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. For Enbrel®, SC Orencia® or SC Actemra®: Failure of two (2) of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Humira®, Simponi Aria®, or Xeljanz®/ Xeljanz XR®;
7. Dose does not exceed maximum dose indicated in background.

Approval duration
Commercial: 12 months
Medicaid: 12 months

J. Psoriatic Arthritis (must meet all)**:**

1. Diagnosis of PsA;
2. Request is for one of the following: Humira®, Cimzia®, Cosentyx®, Enbrel®, Inflectra®, Orencia®, Otezla®, Remicade®, Renflexis™, Simponi®, Simponi Aria®, Stelara®, Taltz®, Tremfya®, Xeljanz®/ Xeljanz XR®;
3. Prescribed by or in consultation with a dermatologist or rheumatologist;
4. Member meets one of the following (a or b):
   a. For Humira®, Cimzia®, Cosentyx®, Enbrel®, Inflectra®, Orencia®, Otezla®, Remicade®, Renflexis™, Simponi®, Stelara®, Taltz®, Tremfya®, Xeljanz®/ Xeljanz XR®: age 18 years of age or older;
   b. For Simponi Aria®: age 2 years of age or older;
5. For Cosentyx®, Enbrel®, Orencia®, Remicade®, or Tremfya®: Failure of a trial of two (2) of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Cimzia®, Humira®, Inflectra®, Otezla®, Renflexis™, Simponi®, Simponi Aria®, Stelara®, Taltz®, or Xeljanz®/ Xeljanz XR®;
6. Dose does not exceed maximum dose indicated in background.

Approval duration
Commercial: 12 months
Medicaid: 12 months

K. Rheumatoid Arthritis (must meet all)**:**

1. Diagnosis of RA;
2. Request is for one of the following: Humira®, Actemra®, Cimzia®, Enbrel®, Inflectra®, Kevzara®, Kineret®, Olumiant®, Orencia®, Remicade®, Renflexis™, Rinvoq™, Simponi®, Simponi Aria®, Xeljanz®/ Xeljanz XR®;
3. Prescribed by or in consultation with a rheumatologist;
4. Age 18 years of age or older;
5. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of MTX at up to maximally indicated doses;
   b. Member has intolerance or contraindication to MTX (see Appendix D), and failure of a ≥ 3 consecutive month trial of at least one conventional DMARD (e.g., sulfasalazine, leflunomide, hydroxychloroquine) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effect are experienced;

6. For Actemra®, Enbrel®, Kevzara®, Kineret®, Olumiant®, Orencia®, Remicade®,: Failure of two (2) of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Humira®, Cimzia®, Inflectra®, Rinvoq™, Renflexis™, Simponi®, Simponi Aria®, or Xeljanz®/ Xeljanz XR®**;**
7. Dose does not exceed maximum dose indicated in background.

Approval duration
Commercial: 12 months
Medicaid: 12 months

L. Systemic Juvenile Idiopathic Arthritis (must meet all)**:**

1. Diagnosis of SJIA;
2. Request is for Actemra®;
3. Prescribed by or in consultation with a dermatologist, rheumatologist, or gastroenterologist;
4. Age 2 years of age or older;
5. Member meets one of the following (a or b):
   a. Failure of a trial of ≥ 3 consecutive months of MTX or leflunomide at up to maximally indicated doses, unless contraindicated or clinically significantadverse effects are experienced;
   b. Failure of a ≥ 2 week trial of a systemic corticosteroid at up to maximally indicated doses, unless contraindicated or clinically significant adverse effectsare experienced;
6. Dose does not exceed maximum dose indicated in background.

Approval duration
Commercial: 12 months
Medicaid: 12 months

M. Ulcerative Colitis (must meet all)**:**

1. Diagnosis of UC;
2. Request is for one of the following: Entyvio®, Humira®, Inflectra®, Remicade®, Renflexis™, Simponi®, or Xeljanz®/Xeljanz XR®;
3. Prescribed by or in consultation with a gastroenterologist;
4. Member meets one of the following (a or b):
   a. For Entyvio®, Humira®, Simponi®, Xeljanz®/Xeljanz XR®: age 18 years of age or older;
   b. For Inflectra®, Remicade®, Renflexis®: age 6 years of age or older;
5. Failure of a trial of ≥ 3 consecutive months of azathioprine, 6-mercaptopurine, or aminosalicylate (e.g., sulfasalazine), at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. For Entyvio®, Remicade®: Failure of two (2) of the following: Inflectra®, Renflexis™, Simponi®, Humira® or Xeljanz®/Xeljanz XR®, each used for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed maximum dose indicated in background.

Approval duration
Commercial: 12 months
Medicaid: 12 months

N. Uveitis (must meet all)**:**

1. Diagnosis of non-infectious intermediate, posterior, or panuveitis;
2. Request is for Humira;
3. Age 2 years of age or older;
4. Prescribed by or in consultation with an ophthalmologist or rheumatologist;

5. Failure of a ≥ 2 week trial of a systemic corticosteroid (e.g., prednisone) at up to maximally indicated doses, unless contraindicated or clinically significantadverse effects are experienced;
6. Failure of a trial of non-biologic immunosuppressive therapy (e.g., azathioprine, methotrexate, mycophenolate mofetil, cyclosporine, tacrolimus, cyclophosphamide, chlorambucil) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed maximum dose indicated in background.

Approval duration
Commercial: 12 months
Medicaid: 12 months

O. Multiple Sclerosis (must meet all)**:**

1. Diagnosis of one of the following (a, b, or c):
   a. Clinically isolated syndrome;
   b. Relapsing-remitting MS, and failure of Gilenya® at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization is required for Gilenya®*
   c. Secondary progressive MS;
2. Request is for Tysabri®;
3. Prescribed by or in consultation with a neurologist;
4. Age 18 years of age or older;
5. Tysabri is not prescribed concurrently with other disease modifying therapies for MS (see Appendix D);
6. Dose does not exceed 300 mg (1 vial) every 4 weeks.

Approval duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):

1. Member meets one of the following (a or b):
   a. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy.;
   b. Documentation supports that member is currently receiving IV Actemra for CAR T cell-induced CRS and member has not yet received 4 total doses;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed maximum dose indicated in background.

Approval duration
For CRS: Up to 4 doses total
For all other indications: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
AS: Ankylosing Spondylitis
BD: Behçet's disease
CAR: Chimeric Antigen Receptor
CD: Crohn's Disease
CINCA: Chronic Infantile Neurological Cutaneous and Articular syndrome
CRS: Cytokine Release Syndrome

DMARDs: Disease-Modifying Antirheumatic Drugs
GCA: Giant Cell Arteritis
HS: Hidradenitis Suppurativa
MS: Multiple Sclerosis
MTX: Methotrexate
NOMID: Neonatal-Onset Multisystem Inflammatory Disease
nr-axSpA: non-radiographic axial spondyloarthritis
NSAIDs: Non-Steroidal Anti-Inflammatory Drugs
PJIA: Polyarticular Juvenile Idiopathic Arthritis
PsO: Plaque Psoriasis
PsA: Psoriatic Arthritis
RA: Rheumatoid Arthritis
SJIA: Systemic Juvenile Idiopathic Arthritis
TNF: Tumor Necrosis Factor
UC: Ulcerative Colitis
UV: Uveitis

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
acitretin (Soriatane®)	**PsO:** 25 or 50 mg PO once daily	50 mg/day
azathioprine (Azasan®, Imuran®)	**RA:** 1 mg/kg/day PO once daily or divided BID **CD*, GCA*, UC*, UV*:** 1.5 – 2 mg/kg/day PO	2.5 mg/kg/day
chlorambucil (Leukeran®)	**UV*:** 0.2 mg/kg PO once daily, then taper to 0.1 mg/kg PO once daily or less	0.2 mg/kg/day
clindamycin (Cleocin®) + rifampin (Rifadin®)	**HS*:** clindamycin 300 mg PO BID and rifampin 300 mg PO BID	clindamycin: 1,800 mg/day rifampin: 600 mg/day
corticosteroids	**CD*:** prednisone 40 mg PO once daily for 2 weeks or IV 50 – 100 mg Q6H for 1 week budesonide (Entocort EC®) 6 – 9 mg PO once daily **GCA*:** Various **SJIA*:** < 0.5 mg/kg/day PO of prednisone or equivalent **UV*:** prednisone 5 – 60 mg/day PO in 1 – 4 divided doses **BD*:** triamcinolone acetonide cream (Orabase® 0.1%)	Various

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Apply topically to the isolated oral ulcer 3 to 4 times daily as needed for pain. prednisone Initial dose: Week 1: 15 mg PO daily; week 2 onwards: 10 mg PO daily tapered over 2-3 weeks Maintenance dose (if recurrent): 5 mg PO daily	
Cuprimine® (d-penicillamine)	**RA*** Initial dose: 125 or 250 mg PO once daily Maintenance dose: 500 – 750 mg/day PO once daily	1,500 mg/day
cyclophosphamide (Cytoxan®)	**UV*:** 1 – 2 mg/kg/day PO	N/A
cyclosporine (Sandimmune®, Neoral®)	**PsO:** 2.5 – 4 mg/kg/day PO divided BID **RA:** 2.5 – 4 mg/kg/day PO divided BID **UV*:** 2.5 – 5 mg/kg/day PO in divided doses	PsO, RA: 4 mg/kg/day UV: 5 mg/kg/day
doxycycline (Acticlate®)	**HS*:** 50 – 100 mg PO BID	300 mg/day
hydroxychloroquine (Plaquenil®)	**RA*** Initial dose: 400 – 600 mg/day PO once daily Maintenance dose: 200 – 400 mg/day PO once daily	600 mg/day
leflunomide (Arava®)	**PJIA*** Weight < 20 kg: 10 mg every other day Weight 20 - 40 kg: 10 mg/day Weight > 40 kg: 20 mg/day **RA:** 100 mg PO once daily for 3 days, then 20 mg PO once daily **SJIA*:** 100 mg PO every other day for 2 days, then 10 mg every other day	PJIA, RA: 20 mg/day SJIA: 10 mg every other day
6-mercaptopurine (Purixan®)	**CD*, UC*:** 50 mg PO once daily or 1 – 2 mg/kg/day PO	2 mg/kg/day
methotrexate	**CD*, UC*:** 15 – 25 mg/week IM or SC **GCA*:** 20 – 25 mg/week PO **PsO:** 10 – 25 mg/week PO or 2.5 mg PO Q12 hr for 3 doses/week **PJIA*:** 10 – 20 mg/m^2/week PO, SC, or IM **RA:** 7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week **SJIA*:** 0.5 – 1 mg/kg/week PO	30 mg/week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	UV*: 7.5 – 20 mg/week PO	
minocycline	**HS*:** 50 – 100 mg PO BID	200 mg/day
mycophenolate mofetil (Cellcept®)	**UV*:** 500 – 1,000 mg PO BID	3 g/day
NSAIDs (e.g., indomethacin, ibuprofen, naproxen, celecoxib)	**AS, nr-axSpA:** Varies	Varies
Pentasa®(mesalamine)	**CD, UC:** 1,000 mg PO QID	4 g/day
Ridaura®(auranofin)	**RA:** 6 mg PO once daily or 3 mg PO BID	9 mg/day (3 mg TID)
sulfasalazine (Azulfidine®)	**PJIA*:** 30-50 mg/kg/day PO divided BID **RA:** 2 g/day PO in divided doses **UC:** <u>Initial dose:</u> Adults: 3 – 4 g/day PO in divided doses (not to exceed Q8 hrs) Pediatrics: 40 – 60 mg/kg/day PO in 3 –6 divided doses <u>Maintenance dose:</u> Adults: 2 g PO once daily Pediatrics: 30 mg/kg/day PO in 4 divided doses	PJIA: 2 g/day RA: 3 g/day UC: 4 g/day
tacrolimus (Prograf®)	**CD*:** 0.27 mg/kg/day PO in divided doses or 0.15 – 0.29 mg/kg/day PO	N/A
sulfasalazine (Azulfidine®)	**UV*:** 0.1-0.15 mg/kg/day PO	
Biologic DMARDs (e.g., Humira®, Enbrel®, Cosentyx®, Remicade®, Simponi Aria®, Otezla®, Xeljanz® /Xeljanz® XR/, Xeljanz® oral Solution Kevzara®)	See Background. Dosing and Administration	See Background. Dosing and Administration
colchicine (Colcrys®)	**BD*:** 1.2 to 1.8 mg PO daily	1.8 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

*Off-label

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):

Drug Name	Contraindication(s)
Actemra®	• Known hypersensitivity to tocilizumab
Cimzia®	• None reported
Cosentyx®	• Serious hypersensitivity reaction to secukinumab or to any of the excipients
Enbrel®	• Patients with sepsis
Entyvio®	• Patients who have had a known serious or severe hypersensitivity reaction to Entyvio or any of its excipients
Humira®	• None reported
Ilumya™	• Serious hypersensitivity reaction to tildrakizumab or to any of the Excipients
Inflectra®, Remicade®, Renflexis™	• Doses > 5 mg/kg in patients with moderate-to-severe heart failure • Previous severe hypersensitivity reaction to infliximab products or known hypersensitivity to inactive components of the product or to any murine proteins.
Kevzara®	• Known hypersensitivity to sarilumab or any of the inactive ingredients
Kineret®	• Known hypersensitivity to E. coli- derived proteins, Kineret, or any components of the product
Olumiant®	• None reported
Orencia®	• None reported
Otezla®	• Known hypersensitivity to apremilast or any of the excipients in the formulation
Rinvoq™	• None reported
Siliq®	• Patients with Crohn's disease
Simponi®, Simponi Aria®	• None reported
Skyrizi™	• None reported
Stelara®	• Clinically significant hypersensitivity to ustekinumab or to any of the excipients
Taltz®	• Serious hypersensitivity reaction to ixekizumab or to any of the excipients.
Tremfya®	• Serious hypersensitivity reactions to guselkumab or to any of the excipients.
Tysabri®	• Patients who have or have had progressive multifocal leukoencephalopathy • Patients who have had a hypersensitivity reaction to natalizumab
Xeljanz®/ Xeljanz® XR/ Xeljanz® oral Solution	• None reported

- Boxed Warning(s):

Drug Name	Contraindication(s)
Actemra®	• Risk of serious infections
Cimzia®	• There is an increased risk of serious infections leading to hospitalization or death including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens. • Lymphoma and other malignancies have been observed.
Cosentyx®	• None reported
Enbrel®	• Serious infections • Malignancies
Entyvio®	• None reported
Humira®	• Serious infections • Malignancies
Ilumya™	• None reported
Inflectra®, Remicade®, Renflexis™	• Malignancy Serious infections
Kevzara®	• Risk of serious infections
Kineret®	None reported
Olumiant®	• Serious infections • Malignancies • Thrombosis
Orencia®	• None reported
Otezla®	• None reported
Rinvoq™	• Serious infections • Malignancies • Thrombosis
Siliq™	• Suicidal ideation and behavior
Simponi®, Simponi Aria®	• Serious infections • Malignancies
Skyrizi™	• None reported
Stelara®	• None reported
Taltz®	• None reported
Tremfya®	• None reported
Tysabri®	• Progressive multifocal leukoencephalopathy
Xeljanz®/ Xeljanz® XR/ Xeljanz® oral Solution	• Serious infections • Malignancies • Mortality • Thrombosis

APPENDIX D: General Information

- Safety:
  - These agents are immunosuppressives and have the potential to increase the risk of infection and reactivate latent, chronic infections. They should not be administered to patients with a clinically important infection. Caution should be used in patients with chronic infections or history of recurrent infection. If patient develops a serious infection these agents should be discontinued.
  - Serious infections were seen in clinical studies with concurrent use of anakinra and another TNF-blocking agent, etanercept, with no added benefit compared to etanercept alone. Because of the nature of the adverse reactions with this combination therapy, similar toxicities may also result from combination of anakinra and other TNF blocking agents.
- Rheumatoid Arthritis:
  - In RA, failure of MTX or DMARD is defined as a contraindication or ≤ 50% decrease in swollen joint count, ≤ 50% decrease in tender joint count, and ≤ 50% decrease in ESR, or ≤ 50% decrease in CRP, or contraindication to at least 3 months of therapy with MTX at doses up to 25 mg per week or maximum tolerated dose.
- Ankylosing Spondylitis:
  - Several AS treatment guidelines call for a trial of 2 or 3 NSAIDs prior to use of an anti- TNF agent. A two year trial showed that continuous NSAID use reduced radiographic progression of AS versus on demand use of NSAID.
- Ulcerative Colitis:
  - For UC maintenance therapy, failure is defined as having two or more exacerbations requiring steroid therapy.
- Polyarticular Juvenile Idiopathic Arthritis:
  - Failure of MTX in PJIA is defined as disease activity remaining moderate to high despite treatment with MTX.
  - In PJIA, response to treatment is reflected by improvement of disease activity level and poor prognostic features including: reduction in the number of active joints, ESR or CRP, Physician global assessment, patient/parent global assessment, arthritis of the hip or cervical spine, positive RF or ACPA, radiographic damage.
- Xeljanz®:
  - Per prescribing information, tofacitinib should not be used in combination with biologic DMARDs [such as anakinra] or potent immunosuppressants such as azathioprine and cyclosporine. As stated in the black box warning, patients treated with tofacitinib are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as MTX or corticosteroids.
  - Use of tofacitinib in combination with biologic DMARDs or potent immunosuppressants such as azathioprine and cyclosporine is not recommended.
  - Do not initiate tofacitinib if absolute lymphocyte count <500 cells/mm3, an absolute neutrophil count (ANC) <1000 cells/mm3 or hemoglobin <9 g/dL.
  - Use of tofacitinib in patients with severe hepatic impairment is not recommended in any patient population.
  - Avoid use of tofacitinib in patients with an active, serious infection, including localized infections
- Stelara®:
  - Ustekinumab is for subcutaneous administration and is intended for use under the guidance and supervision of a physician. After proper training in subcutaneous injection technique, a patient may self-inject with ustekinumab if a physician determines that it is appropriate. Patients should be instructed to follow the directions provided in the Medication Guide.

  - In the PHOENIX 2 trial, dosing intensification of ustekinumab to every 8 weeks didnot result in greater efficacy compared with continuing treatment every 12weeks.
- Neonatal-Onset Multisystem Inflammatory Disease:
  - Other names used for NOMID are as follows: chronic infantile neurological, CINCA, chronic neurologic, cutaneous, and articular syndrome, infantile onset multisystem inflammatory disease, IOMID syndrome, and Prieur-Griscelli syndrome.
- Enbrel®:
  - Off-label indications:
    - Graft vs. Host disease is listed in Micromedex as Class IIa for pediatric patients and etanercept is recommended in most cases.
    - Severe, refractory hidradenitis suppurativa is listed in Micromedex with an evidence rating of Class IIa for adult patients.
- Hidradenitis suppurativa:
  - HS is sometimes referred to as: "acne inversa, acne conglobata, apocrine acne, apocrinitis, Fox-den disease, hidradenitis axillaris, HS, pyodermia sinifica fistulans, Velpeau's disease, and Verneuil's disease."
  - In HS, Hurley stages are used to determine severity of disease. Hurley stage II indicates moderate disease, and is characterized by recurrent abscesses, with sinus tracts and scarring, presenting as single or multiple widely separated lesions. Hurley stage III indicates severe disease, and is characterized by diffuse or near-diffuse involvement presenting as multiple interconnected tracts and abscesses across an entire area.
  - Etanercept has off-label use supported by some efficacy data in severe, refractory HS through retrospective cohort studies and case reports. This off-label indication for etanercept is recommended by Micromedex with a Class IIa recommendation.
- Taltz®:
  - Ixekizumab is currently being studied for the treatment of rheumatoid arthritis, radiographic axial spondyloarthritis, ankylosing spondylitis, and psoriatic arthritis.
- Definition of failure of MTX or DMARDs
  - Failure of a trial of conventional DMARDs:
    - Child-bearing age is not considered a contraindication for use of MTX. Each drug has risks in pregnancy. An educated patient and family planning would allow use of MTX in patients who have no intention of immediate pregnancy.
    - Social use of alcohol is not considered a contraindication for use of MTX. MTX may only be contraindicated if patients choose to drink over 14 units of alcohol per week. However, excessive alcohol drinking can lead to worsening of the condition, so patients who are serious about clinical response to therapy should refrain from excessive alcohol consumption.
- Examples of positive response to therapy may include, but are not limited to:
  - Reduction in joint pain/swelling/tenderness
  - Improvement in ESR/CRP levels
  - Improvements in activities of daily living
- Ulcerative colitis: there is insufficient evidence to support the off-label weekly dosing of adalimumab for the treatment of moderate-to-severe UC. It is the position of RxAdvance Corporation® that the off-label weekly dosing of adalimumab for the treatment of moderate- to-severe UC is investigational and not medically necessary at this time.
  - The evidence from the *post hoc* study of the adalimumab pivotal trial suggests further studies are needed to confirm the benefit of weekly adalimumab dosing for the treatment of UC in patients

with inadequate or loss of therapeutic response to treatment with adalimumab every other week. No large, randomized or prospective studies have been published to support the efficacy of the higher frequency of dosing, while national and international treatment guidelines also do not strongly support dose escalation of adalimumab for UC. The current market consensus is that weekly dosing of adalimumab is not medically necessary due to lack of evidence to support its benefit.

- The following may be considered for medical justification supporting inability to usean immunomodulator for Crohn's disease:
  - Inability to induce short-term symptomatic remission with a 3-month trial ofsystemic glucocorticoids
  - High-risk factors for intestinal complications may include:
    - Initial extensive ileal, ileocolonic, or proximal GI involvement
    - Initial extensive perianal/severe rectal disease
    - Fistulizing disease (e.g., perianal, enterocutaneous, and rectovaginal fistulas)
    - Deep ulcerations
    - Penetrating, stricturing or stenosis disease and/or phenotype
    - Intestinal obstruction or abscess
  - For TNF-inhibitors, high risk factors for postoperative recurrence may include:
    - Less than 10 years duration between time of diagnosis and surgery
    - Disease location in the ileum and colon
    - Perianal fistula
    - Prior history of surgical resection
    - Use of corticosteroids prior to surgery
- Cimzia®:
  - According to the CRADLE, a prospective, postmarketing, multicenter, pharmacokinetic study (n = 17), there were no or minimal certolizumab pegoltransfer from the maternal plasma to breast milk, with a relative infant dose of 0.15% of the maternal dose.
- PsA: According to the 2018 American College of Rheumatology and National Psoriasis Foundation guidelines, TNF inhibitors or oral small molecules (e.g., methotrexate, sulfasalazine, cyclosporine, leflunomide, apremilast) are preferred over other biologics (e.g., interleukin-17 inhibitors or interleukin-12/23 inhibitors) for treatment-naïve disease. TNF inhibitors are also generally recommended over oral small molecules as first-line therapy unless disease is not severe, member prefers oral agents, or TNF inhibitor therapy is contraindicated.
- Otezla is the first and only FDA-approved treatment for oral ulcers associated with Behçet's disease. However, patients included in the pivotal study had prior treatment with at least one non-biologic Behçet's disease therapy, such as, but not limited to, topical corticosteroids, or systemic treatment.
- Tysabri®:
  - Because of the risk of progressive multifocal leukoencephalopathy, Tysabri is only available through a REMS program called the TOUCH® Prescribing Program.
  - Disease-modifying therapies for MS are: glatiramer acetate (Copaxone®, Glatopa®), interferon beta-1a (Avonex®, Rebif®), interferon beta-1b (Betaseron®, Extavia®), peginterferon beta-1a (Plegridy®), dimethyl fumarate (Tecfidera®), fingolimod (Gilenya®), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®), ocrelizumab (Ocrevus™), cladribine (Mavenclad®), and siponimod (Mayzent®).
  - Tysabri® may cause thrombocytopenia. Monitor patients for bleeding abnormalities. Discontinue Tysabri® in patients with thrombocytopenia.
- The American Academy of Neurology 2018 MS guidelines recommend the use of fingolimod,

natalizumab, and alemtuzumab for patients with highly active MS. Definitions of highly active MS vary and can include measures of relapsing activity and MRI markers of disease activity, such as numbers of gadolinium-enhanced lesions.

- For female patients who are actively attempting to conceive:
  - MTX is a pregnancy category X and is absolutely contraindicated in pregnancy and is not recommended for female patients attempting to conceive.
  - Acitretin should not be used in females attempting to conceive because the drug is esterified in fat remaining in the system for up to three (3) years and has the potential to cause birth defects.
  - Cyclosporine is associated with low birth weights; thus, cyclosporine is not appropriate for female patients attempting to conceive.

References

1. Actemra Prescribing Information. South San Francisco, CA: Genentech; May 2020. Available at: https://www.actemra.com/. Accessed January 21, 2021.
2. Cimzia Prescribing Information. Smyrna, GA: UCB, Inc.; September 2019. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=b4c2c9dc-a0bb-4d64-a667-a67ebe88392d&type=display Accessed January 21, 2021.
3. Cosentyx Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2020. Available at: https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/cosentyx.pdf. Accessed January 21, 2021.
4. Enbrel Prescribing Information. Thousand Oaks, CA: Immunex Corporation: March 2020 Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/103795s5574s5577lbl.pdf. Accessed January 21, 2021.
5. Entyvio Prescribing Information. Deerfield, IL: Takeda Pharmaceuticals America Inc.; March 2020. Available at: www.entyviohcp.com. Accessed January 21, 2021.
6. Humira Prescribing Information. North Chicago, IL: AbbVie, Inc.; March 2020. Available at: http://www.rxabbvie.com/pdf/humira.pdf. Accessed January 21, 2021.
7. Ilumya Prescribing Information. Whitehouse Station, NJ: Merck & Co., Inc.; July 2020. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=c6a322bb-51b9-4f0e-8642-62a9682ffcde&type=display Accessed August 22, 2020.
8. Inflectra Prescribing Information. Lake Forest, IL: Hospira, a Pfizer Company; Aug 2020. Available at: http://labeling.pfizer.com/ShowLabeling.aspx?id=9271. Accessed January 21, 2021
9. Kevzara Prescribing Information. Bridgewater, NJ: Sanofi-Aventis U.S. LLC; April 2018. Available at: https://products.sanofi.us/kevzara/kevzara.pdf. January 21, 2021.
10. Kineret Prescribing Information. Stockholm, Sweden: Swedish Orphan Biovitrum AB; June 2018. Available at: http://www.kineretrx.com/pdf/Full-Prescribing-Information-English.pdf. Accessed January 21, 2021.
11. Olumiant Prescribing Information. Indianapolis, IN: Eli Lilly and Company; July 2020. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=866e9f35-9035-4581-a4b1-75a621ab55cf&type=display Accessed January 21, 2021.
12. Orencia Prescribing Information. Princeton, NJ: Bristol-Meyers Squibb Company; June 2020. Available at: http://www.orenciahcp.com/. Accessed January 21, 2021.
13. Otezla Prescribing Information. Summit, NJ: Celgene Corporation; June 2020. Available at http://www.otezla.com/. Accessed January 21, 2021.
14. Remicade Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; May 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/103772s5389s5391s5394lbl.pdf. Accessed January 21, 2021.
15. Renflexis Prescribing Information. Incheon, Republic of Korea: Samsung Bioepis Co., Ltd./Merck Sharp & Dohme

Corp.; February 2020. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=3827e1be-f328-45f7-b113-311b57039f8c&type=display. Accessed January 21, 2021.
16. Rinvoq Prescribing Information. North Chicago, IL: AbbVie Inc.; July 2020. Available at: www.rinvoq.com. Accessed January 21, 2021.
17. Siliq Prescribing Information. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; April 2020. Available at: http://www.valeant.com/Portals/25/Pdf/PI/Siliq-pi.pdf. Accessed January 21, 2021.
18. Simponi Prescribing Information. Horsham, PA; Janssen Biotech; September 2019. Available at: http://www.simponi.com/shared/product/simponi/prescribing-information.pdf. Accessed January 21, 2021.
19. Simponi Aria Prescribing Information. Horsham, PA; Janssen Biotech; September 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125433s030s031lbl.pdf. Accessed January 21, 2021.
20. Skyrizi Prescribing Information. North Chicago, IL: Abbvie Inc. March 2020. Available at: https://www.rxabbvie.com/pdf/skyrizi_pi.pdf. Accessed January 21, 2021.
21. Stelara Prescribing Information. Horsham, PA: Janssen Biotech; July 2020. Available at: www.stelarainfo.com. Accessed January 21, 2021.
22. Taltz Prescribing Information. Indianapolis, IN: Eli Lilly and Company; May 2020. Available at: http://pi.lilly.com/us/taltz-uspi.pdf. Accessed January 21, 2021.
23. Tremfya Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; July 2020. Available at: https://www.tremfyahcp.com/. Accessed January 21, 2021.
24. Tysabri Prescribing Information. Cambridge, MA: Biogen Inc; June 2020. Available at: http://www.tysabri.com. Accessed January 21, 2021.
25. Xeljanz/Xeljanz XR/Xeljanz oral Solution Prescribing Information. New York, NY: Pfizer Labs. October 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/203214s026lbl.pdf. Accessed January 21, 2021.
26. Aletaha D, Neogi T, Silman AJ, et al. 2010 Rheumatoid Arthritis Classification Criteria. Arthritis and Rheumatism September 2010;62(9):2569-2581.
27. Boulos P, Dougados M, MacLeod SM, et al. Pharmacological Treatment of Ankylosing Spondylitis. Drugs. 2005; 65: 2111-2127.
28. Braun J, Davis J, Dougados M, et al. First update of the international ASAS consensus statement for the use of anti-TNF agents in patients with ankylosing spondylitis. Ann Rheum Dis. 2006; 65:316-320.
29. Braun J, van den Berg R, Baraliako X, et al. 2010 Update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. Ann Rheum Dis 2011; 70:896-904.
30. Colombel JF, Sandborn WJ, Rutgeerts P, et.al. Adalimumab for Maintenance of Clinical Response and Remission in Patients With Crohn`s Disease: The CHARM Trial. Gastroenterology 2007; 132:52-65.
31. Lichtenstein GR, Loftus Jr. EV, Isaacs KI, Regueiro MD, Gerson LB, and Sands BE. ACG clinical guideline: management of Crohn's disease in adults. Am J Gastroenterol. 2018; 113:481-517.
32. Menter A, Gottlieb A, Feldman SR, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. J Am Acad Dermatol. 2008; 58:826-850.
33. Menter A, Gottlieb A, Feldman, SR, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 2. Psoriatic arthritis: overview and guidelines of care for treatment with an emphasis on the biologics. J Am Acad Dermatol May 2008; 58(5): 826-50.
34. Menter A, Korman NF, Elmets CA, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4. Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. J Am Acad Dermatol. 10.1016/j.jaad.2009.03.027
35. Menter A, Korman, NJ, Elmets CA, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 3. Guidelines of care for the management and treatment of psoriasis with topical therapies. J Am Acad Dermatol. 2009; 60:643-659.
36. Ward M, Deodhar A, Akl E, 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. Available at: http://www.rheumatology.org. Accessed July 2017.
37. van der Heijde D, Ramiro S, Landewe R, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis. 2017; 76:978- 991. doi:10.1136/annrheumdis-2016-210770.
38. Zochling J, van der Heijde D, Burgos-Vargas, R, et al. ASAS/EULAR recommendations for the management of ankylosing spondylitis. Ann Rheum Dis. 2006; 65:442-452.
39. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. Ann Rheum Dis 2015; 0:1-12. doi:10.1136/annrheumdis-2015-208337
40. Clowse MEB, Forger F, Hwang C, et al. Minimal to no transfer of certolizumab pegol into breast milk: results from CRADLE, a prospective, postmarketing, multicenter, pharmacokinetic study. Ann Rheum Dis 2017; 76:1980-1896. doi:10.1136/annrheumdis- 2017-211384
41. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis. American College of Rheumatology. 2019; 71(1):5-32. doi: 10.1002/art.40726
42. Alikhan A, Sayed C, Alavi A, et al. North American Clinical Management Guidelines for Hidradenitis Suppurativa: a publication from the United States and Canadian Hidradenitis Suppurativa Foundations. Part II: topical, intralesional, and systemic medical management. J Am Acad Dermatol. 2019; pii: S0190-9622(19)30368-8. doi: 10.1016/j.jaad.2019.02.068.
43. Hatemi G, Mahr A, Takeno M, et al. Improvements and correlations in oral ulcers, disease activity, and QOL in behçet's syndrome patients treated with apremilast: a phase 3 randomized, double-blind, placebo-controlled study. Rheumatology, Volume 58, Issue Supplement_2, March 2019, kez062.023, https://doi.org/10.1093/rheumatology/kez062.02
44. Hatemi G, Christensen R, Bang D, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome Annals of the Rheumatic Diseases 2018;77:808-818.
45. Costello K, Halper J, Kalb R, Skutnik L, Rapp R. The use of disease-modifying therapies in multiple sclerosis, principles and current evidence – a consensus paper by the Multiple Sclerosis Coalition. March 2017. Accessed January 21, 2021.
46. Sandborn WJ. Crohn's Disease Evaluation and Treatment: Clinical Decision Tool. Gastroenterology 2014; 147: 702-705.
47. Bernell O, Lapidus A, Hellers G. Risk Factors for Surgery and Postoperative Recurrence in Crohn's Disease. Annals of Surgery. 2000; 231(1): 38-45.
48. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2018; 90(17): 777-788. Full guideline available at: https://www.aan.com/Guidelines/home/GetGuidelineContent/904.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	02/2020	03/06/2020
Policy was reviewed/updated: 1. Clinical policy title was updated. 2. Drug Applied was updated. 3. Line of Business Policy Applies to was updated to "All lines of	10/07/2020	12/07/2020

business". 4. FDA approved indications added: Ankylosing spondylitis and non-radiographic axial spondylitis for Taltz®; PJIA for Xeljanz®, Xeljanz® oral Solution, Simponi Aria®; Psoriatic Arthris for Tremfya®. 5. Initial therapy criteria I.I, J, K- Criteria added for Xeljanz® Xeljanz® XR/Xeljanz® oral Solution 6. Initial therapy criteria I.A.- Criteria added for Taltz®. 7. Initial therapy criteria I.H.4- age criteria updated for Taltz®, Stelara®. 8. Initial therapy criteria I.M.4- criteria added for Mayo Score. 9. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance". 10. Appendix B Verbiage updated to "Below are suggested therapeutic alternatives based…". 11. Appendix D updated. 12. References were reviewed and updated.		
Policy updated: 1. Step therapy medications updated. 2. Added contraindication information for females actively attempting pregnancy. 3. Initial and continued therapy approval durations for all indications except Cytokine Release Syndrome were updated from 6 months to 12 months.	02/20/2021	3/9/2021
Policy was reviewed and updated according to recent formulary updates: 1. Updated Cosentyx indication for nr-axSpA in Background; 2. Added Enbrel and Remicade to criteria I.A.2 based on FDA-approved indications; 3. Added Entyvio, Remicade and Tysabri to criteria I.C.2 based on FDA-approved indications; 4. Added Enbrel and Remicade to criteria I.H.2 based on FDA-approved indications; 5. Added Actemra, Enbrel and Xeljanz XR to criteria I.I.2 based on FDA-approved indications; 6. Added Remicade, Entyvio and Tysabri to the age criteria I.C.5; 7. Added Remicade and Enbrel to the age criteria I.H.4; 8. Added Enbrel, Remicade and Xeljanz XR to criteria I.J.2 based on FDA-approved indications; 9. Added Xeljanz XR, Remicade and Enbrel to the age criteria I.J.4; 10. Added Remicade, Enbrel and Xeljanz XR to criteria I.K.2 based on FDA-approved indications;	03/29/2021	03/30/2021

11. Added Entyvio, Remicade and Xeljanz XR to criteria I.M.2 based on FDA-approved indications; 12. Added Xeljanz XR, Remicade and Entyvio to the age criteria I.M.4; 13. Updated the trial/failure criteria (I.A.6, I.C.6, I.H.6, I.I.6, I.J.5, I.K.6, and I.M.6) according to the drugs' Preferred vs. Non-preferred status.		