Clinical Policy: Biologic DMARDs

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Line of Business: HIM

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

The following are biologic disease-modifying anti-rheumatic drugs (DMARDs) requiring prior authorization: tocilizumab (Actemra®), infliximab-axxq (Avsola™), 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).

FDA Approved Indication(s)

	AS	nr-axSpA	CD	UC	GCA	NOMID	PJIA	SJIA	PsO	PsA	RA	HS	MS	UV	CRS	BD	DIRA
Actemra					x		x[#]	x[#]			x[#]				x[*]		
Avsola	x		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						x
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				

	AS	nr-axSpA	CD	UC	GCA	NOMID	PJIA	SJIA	PsO	PsA	RA	HS	MS	UV	CRS	BD	DIRA
Xeljanz				x			x			x	x						
Xeljanz XR				x						x	x						

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

Contents:

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

It is the policy of health plans affiliated with Centene Corporation® that Actemra, Avsola, 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, and Xeljanz XR are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Axial Spondyloarthritis (must meet all)**:**

1. Diagnosis of AS or nr-axSpA;
2. Request is for one of the following: Avsola, 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;
5. Failure of at least TWO 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 nr-axSpA for Cimzia or Taltz: Failure of **Cosentyx** used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
7. For AS:
   a. For Cimzia, Simponi, Simponi Aria, or Taltz: Failure of ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated: **Humira, Enbrel, Cosentyx**;
   b. For Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from **Inflectra** and **Renflexis**;
8. Dose does not exceed maximum dose indicated in Section V.

Approval duration: 6 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;
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: 6 months

C. Castleman's Disease (off-label) (must meet all)**:**

1. Diagnosis of Castleman's disease;
2. Disease is relapsed/refractory or progressive;
3. Request is for intravenous Actemra;
4. Member is human immunodeficiency virus (HIV)-negative and human herpesvirus 8 (HHV-8)-negative;
5. Prescribed as second-line therapy as a single agent;
6. Request meets one of the following (a or b):*

a. Dose does not exceed 8 mg/kg per infusion every 2 weeks;
b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months or to member's renewal date, whichever is longer

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

1. Diagnosis of CD;
2. Request is for one of the following: Avsola, Humira, Cimzia, Entyvio, 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 clinically significant adverse effects are experienced or all are contraindicated;
   b. Medical justification supports inability to use immunomodulators (*see Appendix E*);
5. Member meets one of the following (a or b):
   a. For Avsola, Humira, Inflectra, Remicade, Renflexis: age ≥ 6 years;
   b. For Cimzia, Entyvio, Stelara, Tysabri: age ≥ 18 years;
6. For Cimzia, Entyvio, or Tysabri: Failure of BOTH of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or both are contraindicated: **Humira** and **Stelara**;
7. For Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from **Inflectra** and **Renflexis**;
8. Request meets one of the following (a or b):
   a. Dose does not exceed maximum dose indicated in Section V;
   b. For Stelara requests, if request is for a dose that exceeds the maximum dose and frequency indicated in Section V, both of the following (i and ii):
      i. Documentation supports inadequate response to a ≥ 3 month trial of the maximum dose indicated in Section V;
      ii. Failure of a trial of ≥ 3 consecutive months of **Humira,** unless contraindicated or clinically significant adverse effects are experienced.

Approval duration: 6 months

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

1. Request is for an intravenous formulation of Actemra;
2. Age ≥ 2 years;
3. Member meets one of the following (a or b):
   a. Member has a scheduled CAR T cell therapy (e.g., Kymriah™, Yescarta™);
   b. Member has developed refractory CRS related to blinatumomab therapy;
4. Request meets one of the following (a or b):*
   a. Dose does not exceed 800 mg per infusion for up to 4 total doses;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: Up to 4 total doses

F. Deficiency of Interleukin-1 Receptor Antagonist (must meet all)**:**
1. Diagnosis of DIRA confirmed by presence of loss-of-function *ILRN* mutations;
2. Request is for Kineret;
3. Prescribed by or in consultation with a rheumatologist;
4. Dose does not exceed maximum dose indicated in Section V.

Approval duration: 6 months

G. 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;
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 clinically significant adverse effects are experienced or all are contraindicated;
6. Dose does not exceed 162 mg SC every week.

Approval duration: 6 months

H. 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;
5. Documentation of Hurley stage II or stage III (*see Appendix D*);
6. Failure of at least TWO of the following, each tried for ≥ 3 consecutive months from different therapeutic classes, at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated:
   a. Systemic antibiotic therapy (e.g., clindamycin, minocycline, doxycycline, rifampin);
   b. Oral retinoids (e.g., acitretin, isotretinoin);
   c. Hormonal treatment (e.g., estrogen-containing combined oral contraceptives, spironolactone);
7. Dose does not exceed maximum dose indicated in Section V.

Approval duration: 6 months

I. 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 Section V.

Approval duration: 6 months

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

1. Diagnosis of PsO and one of the following (a or b):
   a. Request is for Cimzia, Cosentyx, Enbrel, Humira, Ilumya, Otezla, Siliq, Skyrizi, Stelara, Taltz, or Tremfya: PsO is moderate-to-severe as evidenced by involvement of one of the following (i or ii):
      i. ≥ 3% of total body surface area;
      ii. Hands, feet, scalp, face, or genital area;
   b. Request is for Avsola, Inflectra, Remicade, or Renflexis: PsO is chronic-severe as evidenced by involvement of one of the following (i or ii):
      i. ≥ 10% of total body surface area;
      ii. Hands, feet, scalp, face, or genital area;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Member meets one of the following (a, b, c, or d):
   a. For Avsola, Cimzia, Humira, Ilumya, Inflectra, Otezla, Remicade, Renflexis, Siliq, Skyrizi, Tremfya: age ≥ 18 years;
   b. For Enbrel: age ≥ 4 years;
   c. For Stelara: age ≥ 6 years;
   d. For Cosentyx and Taltz: age ≥ 6 years;
4. 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 clinically significant adverse effects are experienced or both are contraindicated;
5. For Ilumya, failure of a trial ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated: **Humira**, **Skyrizi**, **Stelara**, **Tremfya**, **Cosentyx**, **Enbrel**, **Otezla**;
6. For Cimzia, Siliq, or Taltz and age ≥ 18 years: Failure of ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated: **Humira, Skyrizi, Stelara**, **Tremfya**, **Cosentyx**;
7. For Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from **Inflectra** and **Renflexis**;
8. Request meets one of the following (a or b):
   a. Dose does not exceed maximum dose indicated in Section V;
   b. For Stelara requests, if request is for a dose that exceeds the maximum dose and frequency indicated in Section V, both of the following (i and ii):
      i. Documentation supports inadequate response to a ≥ 3 month trial of the maximum dose indicated in Section V;
      ii. Failure of ALL of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: **Humira, Skyrizi, Tremfya**, **Cosentyx.**

Approval duration: 6 months

K. Polyarticular Juvenile Idiopathic Arthritis (must meet all)**:**
1. Diagnosis of PJIA as evidenced by ≥ 5 joints with active arthritis;
2. Request is for one of the following: Actemra, Enbrel, Humira, Orencia, Simponi Aria, or Xeljanz (immediate-release tablets or oral solution);
3. Prescribed by or in consultation with a rheumatologist;
4. Age ≥ 2 years;
5. Documented baseline 10-joint clinical juvenile arthritis disease activity score (cJADAS-10) (*see Appendix K*);
6. Member meets one of the following (a, b, c, or d):
   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*), failure of a ≥ 3 consecutive month trial of leflunomide or sulfasalazine at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
   c. For sacroiliitis/axial spine involvement (i.e., spine, hip), failure of a ≥ 4 week trial of an NSAID at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   d. Documented presence of high disease activity as evidenced by a cJADAS-10 > 8.5 (*see Appendix K*);
7. For Actemra, Orencia, or Simponi Aria: Failure of ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated: **Enbrel, Humira, and Xeljanz**;
8. Dose does not exceed maximum dose indicated in Section V.

Approval duration: 6 months

L. Psoriatic Arthritis (must meet all)**:**
1. Diagnosis of PsA;
2. Request is for one of the following: Avsola, Cimzia, Cosentyx, Enbrel, Humira, Inflectra, Orencia, Otezla, Remicade, Renflexis, Simponi, Simponi Aria, Stelara, Taltz, Tremfya, Xeljanz, or 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 Simponi Aria: Age ≥ 2 years;
   b. For Avsola, Humira, Cimzia, Cosentyx, Enbrel, Inflectra, Orencia, Otezla, Remicade, Renflexis, Simponi, Stelara, Taltz, Tremfya, Xeljanz, and Xeljanz XR: Age ≥ 18 years;
5. For Cimzia, Orencia, Simponi, Simponi Aria, or Taltz: Failure of a trial of ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated: **Humira Enbrel**, **Otezla**, **Cosentyx**, **Stelara**, **Tremfya, Xeljanz/Xeljanz XR;**
6. For Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from **Inflectra** and **Renflexis**;
7. Request meets one of the following (a or b):
   a. Dose does not exceed maximum dose indicated in Section V;

b. For Stelara requests, if request is for a dose that exceeds the maximum dose and frequency indicated in Section V, both of the following (i and ii):
   i. Documentation supports inadequate response to a ≥ 3 month trial of the maximum dose indicated in Section V;
   ii. Failure of ALL of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: **Humira Enbrel**, **Otezla**, **Cosentyx**, **Tremfya, Xeljanz/Xeljanz XR.**

Approval duration: 6 months

M. Rheumatoid Arthritis (must meet all)**:**
1. Diagnosis of RA per American College of Rheumatology (ACR) criteria (*see Appendix H*);
2. Request is for one of the following: Actemra, Avsola, Cimzia, Enbrel, Humira, 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;
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 clinically significant adverse effects are experienced or all are contraindicated;
6. For Cimzia, Kevzara, Kineret, Olumiant, Orencia, Actemra, Simponi, or Simponi Aria: Failure of a trial of ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated: **Humira**, **Enbrel**, **Rinvoq**, **Xeljanz/Xeljanz XR**;
7. For Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from **Inflectra** and **Renflexis**;
8. Documentation of one of the following baseline assessment scores (a or b):
   a. Clinical disease activity index (CDAI) score (*see Appendix I*);
   b. Routine assessment of patient index data 3 (RAPID3) score (*see Appendix J)*;
9. Dose does not exceed maximum dose indicated in Section V.

Approval duration: 6 months

N. 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;
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 clinically significant adverse effects are experienced or both are contraindicated;
b. Failure of a ≥ 2 week trial of a systemic corticosteroid at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

6. Dose does not exceed maximum dose indicated in Section V.

Approval duration: 6 months

O. Systemic Sclerosis – Associated Interstitial Lung Disease (must meet all):

1. Diagnosis of SSc-ILD;
2. Request is for subcutaneous formulation of Actemra;
3. Prescribed by or in consultation with a pulmonologist;
4. Member meets both of the following (a and b):
   a. Pulmonary fibrosis on high-resolution computed tomography (HRCT);
   b. Additional signs of SSc are identified (*see Appendix L)*;
5. Failure of a ≥ 3 consecutive month trial of cyclophosphamide or mycophenolate mofetil, at up to maximally indicated doses, unless both are contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 162 mg every week.

Approval duration: 6 months

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

1. Diagnosis of UC;
2. Request is for one of the following: Avsola, Entyvio, Humira, Inflectra, Remicade, Renflexis, Simponi, Stelara, Xeljanz, Xeljanz XR;
3. Prescribed by or in consultation with a gastroenterologist;
4. Documentation of a Mayo Score ≥ 6 (*see Appendix F*);
5. Member meets one of the following (a or b):
   a. For Entyvio, Simponi, Stelara, Xeljanz, Xeljanz XR: age ≥ 18 years;
   b. For Avsola, Inflectra, Remicade, Renflexis: age ≥ 6 years;
   c. For Humira: age ≥ 5 years;
6. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;
7. For Entyvio, Simponi: Failure of ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated: **Humira**, **Stelara, Xeljanz/Xeljanz XR** ;
8. For Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from **Inflectra** and **Renflexis**;
9. Request meets one of the following (a or b):
   a. Dose does not exceed maximum dose indicated in Section V;
   b. For Stelara requests, if request is for a dose that exceeds the maximum dose and frequency indicated in Section V, both of the following (i and ii):
      i. Documentation supports inadequate response to a ≥ 3 month trial of the maximum dose indicated in Section V;

ii. Failure of BOTH of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: **Humira, Xeljanz/Xeljanz XR**.

Approval duration: 6 months

Q. Uveitis (must meet all)**:**
1. Diagnosis of non-infectious intermediate, posterior, or panuveitis;
2. Request is for Humira;
3. Age ≥ 2 years;
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 significant adverse 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 Section V.

Approval duration: 6 months

R. Multiple Sclerosis (must meet all)**:**
1. Refer to Tysabri MS criteria.

S. Other diagnoses/indications
1. For Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from **Inflectra** and **Renflexis;**
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PA.154 for health insurance marketplace.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   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 meets one of the following (a, b, c, or d):
   a. For RA: Member is responding positively to therapy as evidenced by one of the following (i or ii):
      i. A decrease in CDAI (*see Appendix I*) or RAPID3 (*see Appendix J*) score from baseline;
      ii. Medical justification stating inability to conduct CDAI re-assessment, and submission of RAPID3 score associated with disease severity that is similar to initial CDAI assessment or improved;
   b. For HS: At least a 25% reduction in inflammatory nodules and abscesses;

c. For pJIA: Member is responding positively to therapy as evidenced by a decrease in cJADAS-10 from baseline (*see Appendix K*);
d. For all other indications: Member is responding positively to therapy;

3. If request is for Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from Inflectra and Renflexis;
4. Member meets one of the following (a or b):
   a. If request is for a dose increase, new dose does not exceed maximum dose indicated in Section V;
   b. For Stelara requests, if request is for a dose increase and new maintenance dose exceeds the maximum dose and frequency indicated in Section V, both of the following (i and ii):
      i. Documentation supports inadequate response to a ≥ 3 month trial of the maximum dose indicated in Section V;
      ii. One of the following (1, 2, 3, or 4):
         1. For CD: Failure of a trial of ≥ 3 consecutive months of **Humira** unless contraindicated or clinically significant adverse effects are experienced;
         2. For UC: Failure of BOTH of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or both are contraindicated: **Humira, Xeljanz/Xeljanz XR**;
         3. For PsA: Failure of ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated: **Humira Enbrel**, **Otezla**, **Cosentyx**, T**remfya**, **Xeljanz/Xeljanz XR;**
      i. For PsO: Failure of ALL of the following, each used for ≥ 3 consecutive months, unless clinically significant adverse effects are experienced or all are contraindicated: **Humira, Skyrizi, Tremfya**, **Cosentyx.**

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

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. For Avsola or Remicade, member has experienced clinically significant adverse effects or has a contraindication to excipients from **Inflectra** and **Renflexis**;
2. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
3. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PA.154 for health insurance marketplace.

III. Diagnoses/Indications for which coverage is NOT authorized:
A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – HIM.PA.154 for health insurance marketplace or evidence of coverage documents;
B. Combination use of biological disease-modifying antirheumatic drugs (bDMARDs), including any tumor necrosis factor (TNF) antagonists [Cimzia®, Enbrel®, Simponi®,

Avsola™, Inflectra™, Remicade®, Renflexis™], interleukin agents [Arcalyst® (IL-1 blocker), Ilaris® (IL-1 blocker), Kineret® (IL-1RA), Actemra® (IL-6RA), Kevzara® (IL-6RA), Stelara® (IL-12/23 inhibitor), Cosentyx® (IL-17A inhibitor), Taltz® (IL-17A inhibitor), Siliq™ (IL-17RA), Ilumya™ (IL-23 inhibitor), Skyrizi™ (IL-23 inhibitor), Tremfya® (IL-23 inhibitor)], janus kinase inhibitors (JAKi) [Xeljanz®/Xeljanz® XR, Rinvoq™], anti-CD20 monoclonal antibodies [Rituxan®, Riabni™, Ruxience™, Truxima®, and Rituxan Hycela®], selective co-stimulation modulators [Orencia®], or integrin receptor antagonists [Entyvio®] because of the possibility of increased immunosuppression, neutropenia and increased risk of infection;

C. For Siliq: treatment of patients with Crohn's disease;
D. For Avsola, Inflectra, Remicade and Renflexis: unspecified iridocyclitis (ICD10 H20.9);
E. For Xeljanz/XeljanzXR: alopecia areata (ICD10: L63), also referred to as patchy hairloss.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AS: ankylosing spondylitis
BD: Behçet's disease
CAR: chimeric antigen receptor
CD: Crohn's disease
CDAI: clinical disease activity index
CINCA: chronic infantile neurological, cutaneous and articular syndrome
cJADAS: clinical juvenile arthritis disease activity score
CRS: cytokine release syndrome
DIRA: deficiency of interleukin-1 receptor antagonist
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
RAPID3: routine assessment of patient index data 3
SJIA: systemic juvenile idiopathic arthritis
SSc-ILD: systemic sclerosis-associated interstitial lung disease
TNF: tumor necrosis factor
UC: ulcerative colitis
UV: uveitis

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
acitretin (Soriatane®)	**PsO** 25 or 50 mg PO QD	50 mg/day
azathioprine (Azasan®, Imuran®)	**RA** 1 mg/kg/day PO QD or divided BID	2.5 mg/kg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	CD*, GCA*, UV* 1.5 – 2 mg/kg/day PO	
chlorambucil (Leukeran®)	**UV*** 0.2 mg/kg PO QD, then taper to 0.1 mg/kg PO QD 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 QD for 2 weeks or IV 50 – 100 mg Q6H for 1 week budesonide (Entocort EC®) 6 – 9 mg PO QD **GCA*** Various **SJIA*** < 0.5 mg/kg/day PO of prednisone or equivalent **UC** budesonide (Uceris®) 9 mg PO QD **UV*** prednisone 5 – 60 mg/day PO in 1 – 4 divided doses **BD*** triamcinolone acetonide cream (Orabase® 0.1%) Apply topically to the isolated oral ulcer 3 to 4 times daily as needed for pain. prednisone <u>Initial dose:</u> Week 1: 15 mg PO daily Week 2 onwards: 10 mg PO daily tapered over 2-3 weeks <u>Maintenance dose (if recurrent):</u> 5 mg PO daily	Various
Cuprimine®	**RA***	1,500 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
(d-penicillamine)	Initial dose: 125 or 250 mg PO QD Maintenance dose: 500 – 750 mg/day PO QD	
cyclophosphamide (Cytoxan®)	**UV*** 1 – 2 mg/kg/day PO **SSc-ILD*** PO: 1 – 2 mg/kg/day IV: 600 mg/m^2/month	PO: 2 mg/kg/day IV: 600 mg/m^2/month
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
Hormonal agents (e.g., estrogen-containing combined oral contraceptives, spironolactone)	**HS** varies	varies
hydroxychloroquine (Plaquenil®)	**RA*** Initial dose: 400 – 600 mg/day PO QD Maintenance dose: 200 – 400 mg/day PO QD	600 mg/day
Isotretinoin (Absorica®, Amnesteem®, Claravis®, Myorisan®, Zenatane®)	**HS** varies	varies 1.6 to 2 mg/kg/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 QD for 3 days, then 20 mg PO QD	PJIA, RA: 20 mg/day SJIA: 10 mg every other day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	SJIA* 100 mg PO every other day for 2 days, then 10 mg every other day	
6-mercaptopurine (Purixan®)	**CD*** 50 mg PO QD or 1 – 2 mg/kg/day PO	2 mg/kg/day
methotrexate (Rheumatrex®)	**CD*** 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 **UV*** 7.5 – 20 mg/week PO	30 mg/week
minocycline (Minocin®)	**HS*** 50 – 100 mg PO BID	200 mg/day
mycophenolate mofetil (Cellcept®)	**UV*** 500 – 1,000 mg PO BID **SSc-ILD*** PO: 1 – 3 g/day	3 g/day
NSAIDs (e.g., indomethacin, ibuprofen, naproxen, celecoxib)	**AS, nr-axSpA, PJIA*** Varies	Varies
Pentasa® (mesalamine)	**CD** 1,000 mg PO QID	4 g/day
Ridaura® (auranofin)	**RA** 6 mg PO QD or 3 mg PO BID	9 mg/day (3 mg TID)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
sulfasalazine (Azulfidine®)	**PJIA*** 30-50 mg/kg/day PO divided BID **RA** 2 g/day PO in 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 **UV*** 0.1-0.15 mg/kg/day PO	N/A
Biologics DMARDs (e.g., Humira, Enbrel, Cosentyx, Remicade, Simponi Aria, Otezla, Xeljanz/Xeljanz XR, Kevzara)	See Section V. Dosing and Administration	See Section V. 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

Drug Name	Contraindication(s)	Boxed Warning(s)
Actemra	Known hypersensitivity to Actemra	Risk of serious infections
Cimzia	None reported	• 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. • Epstein Barr Virus-associated post-transplant lymphoproliferative disorder has been observed.
Cosentyx	Serious hypersensitivity reaction to secukinumab or to any of the excipients	None reported
Enbrel	Patients with sepsis	• Serious infections • Malignancies

Drug Name	Contraindication(s)	Boxed Warning(s)
Entyvio	Patients who have had a known serious or severe hypersensitivity reaction to Entyvio or any of its excipients	None reported
Humira	None reported	• Serious infections • Malignancies
Ilumya	Serious hypersensitivity reaction to tildrakizumab or to any of the excipients	None reported
Avsola, Inflectra, Remicade, Renflexis	• Doses > 5 mg/kg in patients with moderate-to-severe heart failure • Re-administration to patients who have experienced a severe hypersensitivity reaction to infliximab products • Known hypersensitivity to inactive components of the product or to any murine proteins	• Serious infections • Malignancy
Kevzara	Known hypersensitivity to sarilumab or any of the inactive ingredients	Risk of serious infections
Kineret	Known hypersensitivity to *E. coli*-derived proteins, Kineret, or any components of the product	None reported
Olumiant	None reported	• Serious infections • Malignancies • Thrombosis
Orencia	None reported	None reported
Otezla	Known hypersensitivity to apremilast or to any of the excipients in the formulation	None reported
Rinvoq	None reported	• Serious infections • Malignancies • Thrombosis
Siliq	Patients with Crohn's disease	Suicidal ideation and behavior
Simponi, Simponi Aria	None reported	• Serious infections • Malignancies
Skyrizi	None reported	None reported
Stelara	Clinically significant hypersensitivity to ustekinumab or any of its excipients	None reported
Taltz	Previous serious hypersensitivity reaction, such as anaphylaxis, to	None reported

Drug Name	Contraindication(s)	Boxed Warning(s)
	ixekizumab or to any of the excipients	
Tremfya	None reported	None reported
Tysabri	• Patients who have or have had progressive multifocal leukoencephalopathy • Patients who have had a hypersensitivity reaction to Tysabri	• Progressive multifocal leukoencephalopathy
Xeljanz/ Xeljanz XR	None reported	• 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. • Epstein Barr Virus-associated post-transplant lymphoproliferative disorder has been observed. • Rheumatoid arthritis patients with at least one cardiovascular risk factor had a higher rate of all-cause mortality and thrombosis with Xeljanz 10 mg twice daily vs. 5 mg twice daily or TNF blockers.

Appendix D: General Information

- 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:

  - For Ulcerative Colitis maintenance therapy, failure is defined as having two or more exacerbations requiring steroid therapy.
- Stelara:
  - In the PHOENIX 2 trial, dosing intensification of Stelara to every 8 weeks did not result in greater efficacy compared with continuing treatment every 12 weeks.
- 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.
- 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.
  - Enbrel 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 Enbrel is recommended by Micromedex with a Class IIa recommendation.
- Ulcerative colitis: there is insufficient evidence to support the off-label weekly dosing of Humira for the treatment of moderate-to-severe UC. It is the position of Centene Corporation® that the off-label weekly dosing of Humira 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 Humira pivotal trial suggests further studies are needed to confirm the benefit of weekly Humira dosing for the treatment of UC in patients with inadequate or loss of therapeutic response to treatment with Humira 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 Humira for UC. The current market consensus is that weekly dosing of Humira is not medically necessary due to lack of evidence to support its benefit.
- Cimzia:
  - According to the CRADLE, a prospective, postmarketing, multicenter, pharmacokinetic study (n = 17), there were no or minimal certolizumab pegol transfer from the maternal plasma to breast milk, with a relative infant dose of 0.15% of the maternal dose.
- Nr-axSpA: guideline recommendations are largely extrapolated from evidence in AS.
- Infliximab used in the treatment of unspecified iridocyclitis (anterior uveitis) has primarily been evaluated in case reports and uncontrolled case series. One phase II clinical trial by Suhler and associates (2009) reported the 2-year follow-up data of patients with refractory uveitis treated with intravenous infliximab as part of a prospective clinical trial. Their 1-year data, published in 2005 (Suhler, 2005) reported reasonable initial success, but an unexpectedly high incidence of adverse events. Of their

23 patients, 7 developed serious adverse events, including 3 thromboses, 1 malignancy, 1 new onset of congestive heart failure, and 2 cases of drug-induced lupus. The American Optometric Association anterior uveitis clinical practice guidelines recommend alternative therapies that include ophthalmic corticosteroids (e.g., prednisolone, dexamethasone, fluoromethalone) and anticholinergics (e.g., atropine, cyclopentolate, homatropine). If the disease has not responded to topical therapy, oral corticosteroids can be considered.

- Because of the risk of progressive multifocal leukoencephalopathy, Tysabri is only available through a REMS program called the TOUCH® Prescribing Program.

Appendix E: Immunomodulator Medical Justification

- The following may be considered for medical justification supporting inability to use an immunomodulator for Crohn's disease:
  - Inability to induce short-term symptomatic remission with a 3-month trial of systemic 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

Appendix F: Mayo Score

- Mayo Score: evaluates ulcerative colitis stage, based on four parameters: stool frequency, rectal bleeding, endoscopic evaluation and Physician's global assessment. Each parameter of the score ranges from zero (normal or inactive disease) to 3 (severe activity) with an overall score of 12.

Score	Decoding
0 – 2	Remission
3 – 5	Mild activity
6 – 10	Moderate activity
>10	Severe activity

- The following may be considered for medical justification supporting inability to use an immunomodulator for ulcerative colitis:
  - Documentation of Mayo Score 6 – 12 indicative of moderate to severe ulcerative colitis.

Appendix G: Dose Rounding Guidelines for Weight-Based Doses

Actemra for Intravenous Use for PJIA and SJIA

Weight-based Dose Range	Vial Quantity Recommendation
≤ 83.99 mg	1 vial of 80 mg/4 mL
84 to 209.99 mg	1 vial of 200 mg/10 mL
210 to 419.99 mg	1 vial of 400 mg/20 mL
420 to 503.99 mg	1 vial of 80 mg/4 mL and 1 vial 400 mg/20 mL
504 to 629.99 mg	1 vial of 200 mg/10 mL and 1 vial 400 mg/20 mL
630 to 839.99 mg	2 vials 400 mg/20 mL
840 to 923.99 mg	1 vial of 80 mg/4 mL and 2 vials 400 mg/20 mL
924 to 1,049.99 mg	1 vial of 200 mg/10 mL and 2 vials 400 mg/20 mL
1050 to 1,259.99 mg	3 vials 400 mg/20 mL

Enbrel for PJIA and Pediatric PsO

Weight-based Dose Range	Vial Quantity Recommendation
≤ 25.99 mg	1 vial of 25 mg/0.5 mL
26 to 52.49 mg	1 vial of 50 mg/mL

Infliximab for All Indications

Weight-based Dose Range	Vial Quantity Recommendation
≤ 104.99 mg	1 vial of 100 mg/20 mL
105 to 209.99 mg	2 vials of 100 mg/20 mL
210 to 314.99 mg	3 vials of 100 mg/20 mL
315 to 419.99 mg	4 vials of 100 mg/20 mL
420 to 524.99 mg	5 vials of 100 mg/20 mL
525 to 629.99 mg	6 vials of 100 mg/20 mL
630 to 734.99 mg	7 vials of 100 mg/20 mL
735 to 839.99 mg	8 vials of 100 mg/20 mL

Kineret for NOMID

Weight-based Dose Range	Vial Quantity Recommendation
≤ 104.99 mg	1 syringe of 100 mg/0.67 mL
105 to 209.99 mg	2 syringes of 100 mg/0.67 mL
210 to 314.99 mg	3 syringes of 100 mg/0.67 mL
315 to 419.99 mg	4 syringes of 100 mg/0.67 mL
420 to 524.99 mg	5 syringes of 100 mg/0.67 mL
525 to 629.99 mg	6 syringes of 100 mg/0.67 mL
630 to 734.99 mg	7 syringes of 100 mg/0.67 mL
735 to 839.99 mg	8 syringes of 100 mg/0.67 mL

Orencia for Intravenous Use PJIA and SJIA

Weight-based Dose Range	Vial Quantity Recommendation
≤ 262.49 mg	1 vial of 250 mg
262.50 mg to524.99 mg	2 vials of 250 mg
525 to 787.49 mg	3 vials of 250 mg
787.50 mg to 1,049.99 mg	4 vials of 250 mg

Orencia for Subcutaneous Use for PJIA and SJIA

Weight-based Dose Range	Prefilled Syringe Quantity Recommendation
10 to 24.99 kg	1 syringe of 50 mg/0.4 mL
25 to 49.99 kg	1 syringe of 87.5 mg/0.7 mL
> 50 kg	1 syringe of 125 mg/mL

Simponi Aria for All Indications

Weight-based Dose Range	Vial Quantity Recommendation
≤ 52.49 mg	1 vial of 50 mg/4 mL
52.5 to 104.99 mg	2 vials of 50 mg/4 mL
105 to 157.49 mg	3 vials of 50 mg/4 mL
157.5 to 209.99 mg	4 vials of 50 mg/4 mL
210 to 262.49 mg	5 vials of 50 mg/4 mL

Stelara for PsO

Weight-based Dose Range	Quantity Recommendation
Subcutaneous, Syringe	
≤ 46.99 mg	1 syringe of 45 mg/0.5 mL
47 to 94.49 mg	1 syringe of 90 mg/1 mL
94.5 to 141.49 mg	1 syringe of 45 mg/0.5 mL and 1 syringe of 90 mg/1 mL
Subcutaneous, Vial	
≤ 46.99 mg	1 vial of 45 mg/0.5 mL
47 to 94.49 mg	2 vials of 45 mg/0.5 mL
Intravenous, Vial	
94.5 to 136.49 mg	1 vial of 130 mg/26 mL

Appendix H: The 2010 ACR Classification Criteria for RA
Add score of categories A through D; a score of ≥ 6 out of 10 is needed for classification of a patient as having definite RA.

A	**Joint involvement**	Score
	1 large joint	0
	2-10 large joints	1
	1-3 small joints (with or without involvement of large joints)	2
	4-10 small joints (with or without involvement of large joints)	3
	> 10 joints (at least one small joint)	5
B	**Serology (at least one test result is needed for classification)**	
	Negative rheumatoid factor (RF) *and* negative anti-citrullinated protein antibody (ACPA)	0
	Low positive RF *or* low positive ACPA * *Low: < 3 x upper limit of normal*	2
	High positive RF *or* high positive ACPA * *High: ≥ 3 x upper limit of normal*	3

C	**Acute phase reactants (at least one test result is needed for classification)**	
	Normal C-reactive protein (CRP) and normal erythrocyte sedimentation rate (ESR)	0
	Abnormal CRP or abnormal ESR	1
D	**Duration of symptoms**	
	< 6 weeks	0
	≥ 6 weeks	1

Appendix I: Clinical Disease Activity Index (CDAI) Score
The Clinical Disease Activity Index (CDAI) is a composite index for assessing disease activity in RA. CDAI is based on the simple summation of the count of swollen/tender joint count of 28 joints along with patient and physician global assessment on VAS (0–10 cm) Scale for estimating disease activity. The CDAI score ranges from 0 to 76.

CDAI Score	Disease state interpretation
≤ 2.8	Remission
> 2.8 to ≤ 10	Low disease activity
> 10 to ≤ 22	Moderate disease activity
> 22	High disease activity

Appendix J: Routine Assessment of Patient Index Data 3 (RAPID3) Score
The Routine Assessment of Patient Index Data 3 (RAPID3) is a pooled index of the three patient-reported ACR core data set measures: function, pain, and patient global estimate of status. Each of the individual measures is scored 0 – 10, and the maximum achievable score is 30.

RAPID3 Score	Disease state interpretation
≤ 3	Remission
3.1 to 6	Low disease activity
6.1 to 12	Moderate disease activity
> 12	High disease activity

Appendix K: Clinical Juvenile Arthritis Disease Activity Score based on 10 joints (cJADAS-10)
The cJADAS10 is a continuous disease activity score specific to JIA and consisting of the following three parameters totaling a maximum of 30 points:

- Physician's global assessment of disease activity measured on a 0-10 visual analog scale (VAS), where 0 = no activity and 10 = maximum activity;
- Parent global assessment of well-being measured on a 0-10 VAS, where 0 = very well and 10 = very poor;
- Count of joints with active disease to a maximum count of 10 active joints*

**ACR definition of active joint: presence of swelling (not due to currently inactive synovitis or to bony enlargement) or, if swelling is not present, limitation of motion accompanied by pain, tenderness, or both*

cJADAS-10	Disease state interpretation
≤ 1	Inactive disease
1.1 to 2.5	Low disease activity
2.51 to 8.5	Moderate disease activity

cJADAS-10	Disease state interpretation
> 8.5	High disease activity

Appendix L: American College of Rheumatology (ACR) 2013 SSc Classification Criteria
While the majority of patients with SSc experience skin thickening and variable involvement of internal organs, there is no one confirmatory test for SSc. Similar to the IPF guidelines above, ACR lists HRCT as a diagnostic method for determining pulmonary fibrosis in SSc-ILD. The other diagnostic parameters below are drawn from ACR's scoring system purposed for clinical trials. While informative, ACR cautions that the scoring system parameters are not all inclusive of the myriad of SSc manifestations that may occur across musculoskeletal, cardiovascular, renal, neuromuscular and genitourinary systems.

Examples of SSc skin/internal organ manifestations and associated laboratory tests:
- Skin thickening of the fingers
- Fingertip lesions
- Telangiectasia
- Abnormal nailfold capillaries
- Raynaud's phenomenon
- SSc-ILD
- Pulmonary arterial hypertension
- SSc-related autoantibodies
- Anticentromere
- Anti-topoisomerase I (anti-Scl-70)
- Anti-RNA polymerase III

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Abatacept (Orencia)* **Also see Appendix G: Dose Rounding Guidelines for Weight-Based Doses*	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 SC: weight-based dose once weekly	IV: 1,000 mg every 4 weeks SC: 125 mg/week

Drug Name	Indication	Dosing Regimen	Maximum Dose
		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 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	40 mg every other week
	UC	Initial dose: *Adults: 160* mg SC on Day 1, then 80 mg SC on Day 15 *Pediatrics:*	*Adults:* 40 mg every other week

<table>
<tr><th>Drug Name</th><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td></td><td></td><td>
<table>
<tr><th>Weight</th><th>Days 1 through 15</th></tr>
<tr><td>20 kg to less than 40 kg</td><td>Day 1: 80 mg
Day 8: 40 mg
Day 15: 40 mg</td></tr>
<tr><td>40 kg and greater</td><td>Day 1: 160 mg (single dose or split over tw consecutive days
Day 8: 80 mg
Day 15: 80 mg</td></tr>
</table>
<u>Maintenance dose:</u>
Adults: 40 mg SC every other week starting on Day 29

Pediatrics:
<table>
<tr><th>Weight</th><th>Starting on Day 29*</th></tr>
<tr><td>20 kg to less than 40 kg</td><td>40 mg every other week or 20 mg every week</td></tr>
<tr><td>40 kg and greater</td><td>80 mg every other week or 40 mg every week</td></tr>
</table>
*Continue the recommended pediatric dosage in patients who turn 18 years of age and who are well-controlled on Humira regimen.
</td><td>Pediatrics:
80 mg every other week or 40 mg every week</td></tr>
<tr><td></td><td>PsO</td><td><u>Initial dose:</u>
80 mg SC
<u>Maintenance dose:</u>
40 mg SC every other week starting one week after initial dose</td><td>40 mg every other week</td></tr>
<tr><td></td><td>UV</td><td>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

Adults:
Initial dose of 80 mg SC, followed by 40 mg SC every other week starting one week after the initial dose</td><td>40 mg every other week</td></tr>
<tr><td></td><td>HS</td><td>For patients 12 years of age and older weighing at least 30 kg:
<u>Initial dose:</u></td><td>40 mg/week</td></tr>
</table>

Drug Name	Indication	Dosing Regimen	Maximum 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	
Anakinra (Kineret)* **Also see Appendix G: Dose Rounding Guidelines for Weight-Based Doses*	RA	100 mg SC QD	100 mg/day
	NOMID	Initial dose: 1 – 2 mg/kg SC QD or divided BID Maintenance dose: 8 mg/kg SC QD or divided BID	8 mg/kg/day
	DIRA	Initial dose: 1 – 2 mg/kg SC QD Maintenance dose: Adjust doses in 0.5 to 1 mg/kg increments.	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 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	60 mg/day
Baricitinib (Olumiant)	RA	2 mg PO QD	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	400 mg every 4 weeks

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Maintenance dose: 400 mg SC 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)* **Also see Appendix G: Dose Rounding Guidelines for Weight-Based Doses*	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

Drug Name	Indication	Dosing Regimen	Maximum Dose
*Also see Appendix G: Dose Rounding Guidelines for Weight-Based Doses	pJIA	Initial dose: 80 mg/m^2 at weeks 0 and 4 Maintenance dose: 80 mg/m^2 IV every 8 weeks	80 mg/m^2 IV every 8 weeks
Guselkumab (Tremfya)	PsA PsO	Initial dose: 100 mg SC at weeks 0 and 4 Maintenance dose: 100 mg SC every 8 weeks	100 mg every 8 weeks
Infliximab (Avsola, Inflectra, Remicade, Renflexis)* *Also see Appendix G: Dose Rounding Guidelines for Weight-Based Doses	CD, UC	Initial dose: *Adults/Pediatrics:* 5 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: *Adults/Pediatrics:* 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
	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	Adults: Initial dose:	80 mg every 4 weeks

<table>
<tr><th>Drug Name</th><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td></td><td>coexistent PsA)</td><td>160 mg (two 80 mg injections) SC at week 0, then 80 mg SC at weeks 2, 4, 6, 8, 10, and 12
<u>Maintenance dose:</u>
80 mg SC every 4 weeks

<u>Pediatrics between ages of 6 and 18 years:</u>
<table>
<tr><th>Pediatric Patient's Weight</th><th>Starting Dose (Week 0)</th><th>Dose every 4 weeks (Q4W) Thereafter</th></tr>
<tr><td>> 50 kg</td><td>160 mg (two 80 mg injections)</td><td>80 mg</td></tr>
<tr><td>25 to 50 kg</td><td>80 mg</td><td>40 mg</td></tr>
<tr><td>< 25 kg</td><td>40 mg</td><td>20 mg</td></tr>
</table></td><td></td></tr>
<tr><td></td><td>PsA, AS</td><td><u>Initial dose:</u> 160 mg (two 80 mg injections) SC at week 0
<u>Maintenance dose:</u>
80 mg SC every 4 weeks</td><td>80 mg every 4 weeks</td></tr>
<tr><td></td><td>nr-axSpA</td><td><u>80 mg SC every 4 weeks</u></td><td>80 mg every 4 weeks</td></tr>
<tr><td>Natalizumab (Tysabri)</td><td>MS, CD</td><td>300 mg IV every 4 weeks</td><td>300 mg/4 weeks</td></tr>
<tr><td>Risankizumab-rzaa (Skyrizi)</td><td>PsO</td><td>150 mg SC at weeks 0, 4, and every 12 weeks thereafter</td><td>150 mg/12 weeks</td></tr>
<tr><td>Sarilumab (Kevzara)</td><td>RA</td><td>200 mg SC once every two weeks</td><td>200 mg/2 weeks</td></tr>
<tr><td>Secukinumab (Cosentyx)</td><td>PsO (with or without PsA)</td><td>Adults: 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)

Pediatric patients age 6 to 17 years and weight < 50 kg (PsO only): 75 mg SC at weeks 0, 1, 2, 3 and 4, followed by maintenance dose of 75 mg every 4 weeks

Pediatric patients age 6 to 17 years and weight ≥ 50 kg (PsO only): 150 mg SC at weeks 0, 1, 2, 3 and 4, followed by maintenance dose of 150 mg every 4 weeks</td><td>Adults: 300 mg every 4 weeks

Pediatric patients: 150 mg every 4 weeks</td></tr>
</table>

Drug Name	Indication	Dosing Regimen	Maximum Dose
	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 arthritis, consider a dosage of 300 mg.	300 mg every 4 weeks
	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 For AS only: if a patient continues to have active ankylosing spondylitis, consider a dosage of 300 mg SC every 4 weeks.	AS: 300 mg every 4 weeks nr-axSpA: 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 Ilumya should only be administered by a healthcare professional.	100 mg every 12 weeks
Tocilizumab (Actemra)* **Also see Appendix G: Dose Rounding Guidelines for Weight-Based Doses*	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

Drug Name	Indication	Dosing Regimen	Maximum Dose
	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 infusion 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
	SSc-ILD	162 mg SC once weekly	SC: 162 mg every week
Tofacitinib (Xeljanz)	pJIA	• 10 kg ≤ body weight < 20 kg: 3.2 mg (3.2 mL oral solution) PO BID • 20 kg ≤ body weight < 40 kg: 4 mg (4 mL oral solution) PO BID • Body weight ≥ 40 kg: 5 mg PO BID	10 mg/day
	PsA RA	5 mg PO BID	
	UC	Induction: 10 mg PO BID for 8 weeks, up to 16 weeks Maintenance: 5 mg PO BID	Induction: 20 mg/day Maintenance: 10 mg/day
Tofacitinib extended-release (Xeljanz XR)	PsA RA	11 mg PO QD	11 mg/day
	UC	Induction: 22 mg PO QD for 8 weeks, up to 16 weeks Maintenance: 11 mg PO QD	Induction: 22 mg/day Maintenance: 11 mg/day
Upadacitinib (Rinvoq)	RA	15 mg PO QD	15 mg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
Ustekinumab (Stelara)* *Also see Appendix G: Dose Rounding Guidelines for Weight-Based Doses*	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 6 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 UC	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
Vedolizumab (Entyvio)	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

VI. Product Availability

Drug Name	Availability
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)	**Tablet:** 1 mg, 2 mg

Drug Name	Availability
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 **Single-dose vial:** 25 mg/0.5 mL **Multi-dose vial for reconstitution:** 25 mg **Enbrel Mini™ single-dose prefilled cartridge for use with AutoTouch™ 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-axxq (Inflectra)	**Single-use vial**: 100 mg/20 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 **Single-dose One-Press pen-injector**: 100 mg/mL
Natalizumab (Tysabri)	**Single-use vial**: 300 mg/15 mL
Risankizumab-rzaa (Skyrizi)	**Single-dose prefilled syringe:** 75 mg/0.83 mL, 150 mg/mL **Single-dose prefilled pen:** 150 mg/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:** 75 mg/0.5 mL, 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)	**Tablets**: 5 mg, 10 mg **Oral solution**: 1 mg/mL

Drug Name	Availability
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

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Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0129	Injection, abatacept, 10 mg
J0135	Injection, adalimumab, 20 mg
J0717	Injection, certolizumab pegol, 1 mg
J1438	Injection, etanercept, 25 mg
J1602	Injection, golimumab, 1 mg, for intravenous use
J1628	Injection, guselkumab, 1 mg
J1745	Injection, infliximab, excludes biosimilar, 10 mg
J2323	Injection, natalizumab, 1 mg
J3590	Injection, risankizumab-rzaa, ## mg
J3245	Injection, tildrakizumab, 1 mg
J3262	Injection, tocilizumab, 1 mg
J3357	Ustekinumab, for subcutaneous injection,1 mg
J3358	Ustekinumab, for intravenous injection, 1 mg
J3380	Injection, vedolizumab, 1 mg
Q5103	Injection, infliximab-dyyb, biosimilar, (inflectra), 10 mg
Q5104	Injection, infliximab-abda, biosimilar, (renflexis), 10 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created; per SDC and prior clinical guidance adapted from CP.CPA.194; replaces the following policies where HIM line of business has been removed: CP.PHAR.241, CP.PHAR.242, CP.PHAR.244, CP.PHAR.247, CP.PHAR.250, CP.PHAR.253, CP.PHAR.254, CP.PHAR.257, CP.PHAR.261, CP.PHAR.263, CP.PHAR.264, CP.PHAR.267, CP.PHAR.346, CP.PHAR.364, CP.PHAR.375, CP.PHAR.386; the following HIM policies are being retired: HIM.PA.SP17, HIM.PA.SP38.	12.11.19	02.20
Criteria added for new FDA indication for Taltz: ankylosing spondylitis; criteria added for new FDA indication for Stelara: ulcerative colitis; removed redirection to azathioprine, 6-	12.03.19	02.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
mercaptopurine, or aminosalicylate for UC per 2019 ACG guidelines; references reviewed and updated. RT4: added Xeljanz XR 22 mg dose form and updated to indicate FDA approved use and dosing in UC with similar redirection as Xeljanz immediate release; added Tremfya pen-injector dose form. Added unspecified iridocyclitis to Section III as an excluded use for Inflectra, Remicade, and Renflexis. Added Coding Implications table.		
2Q 2020 annual review: for RA, added specific diagnostic criteria for definite RA, baseline CDAI score requirement, and decrease in CDAI score as positive response to therapy; for UC, added Mayo score requirement of at least 6; allowed IV Actemra for refractory CRS related to blinatumomab therapy per NCCN; added dose rounding guidelines for agents (i.e., Actemra, Enbrel, infliximab, Kineret, Orencia, Stelara, Simponi Aria) with weight-based doses; added NCCN supported off-label uses for Actemra; added age limit of 2 year or older for Actemra for CRS; added requirement for redirection to Inflectra and Renflexis to Section II for Remicade; for HS, revised requirement from systemic antibiotics to additionally require oral retinoids or hormonal therapy, and required at least a 25% reduction in inflammatory nodules and abscesses for reauthorization; added pediatric age extension for Taltz from age 18 years down to 6 years old; removed criteria set for Tysabri for MS; refer to HIM.PA.SP17; references reviewed and updated.	04.23.20	05.20
Per April SDC and prior clinical guidance, added Skyrizi as a preferred product for PsO, added Rinvoq as a preferred product for RA.	04.22.20	
Per July SDC and prior clinical guidance, added Stelara and Tremfya as preferred products for their respective indications; revised redirection for AS, PsA, PsO, and RA to require ALL among the list of preferred products; for Stelara off-label dosing added requirement for documentation of inadequate response on a 3 month trial of maximum indicated dose and redirection to alternative preferred products; for SC Actemra RA requests, removed existing redirection to Kevzara; for Cimzia, Entyvio, or Tysabri CD requests revised redirection to require Humira and Stelara; for Entyvio and Simponi UC request revised redirection to require Humira, Stelara, and Xeljanz/Xeljanz XR.	07.09.20	
RT2: Added newly FDA-approved indication for Cosentyx and Taltz for nr-axSpA to the policy, including requiring redirection only to Cosentyx based on contracting (no redirection to Humira and Enbrel as these are off-label for nr-axSpA), while allowing for redirection to Cosentyx, Humira, and Enbrel when the diagnosis is AS; added new FDA indication for Tremfya: PsA; RT4: updated Enbrel new dosage	08.25.20	11.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
form: single-dose vial AND updated Stelara PsO criteria and dosing information in response to pediatric extension to be used in patients 6yo+; references reviewed and updated.		
Per November SDC and prior clinical guidance, added redirection to Inflectra and Renflexis for Avsola; Revised typo in Appendix E from "normal ESR" to "abnormal ESR" for a point gained for ACR Classification Criteria.	11.22.20	
RT2: Added newly FDA-approved indication for Simponi Aria: pJIA and Xeljanz: pcJIA; removed duplication of information included in Appendix D: General Information as well as information that did not aid in decision-making; RT4: updated Xeljanz new dosage form: oral solution; updated Simponi for PsA given age extension to pediatrics; references reviewed and updated. Added criteria for RAPID3 assessment for RA given limited in-person visits during COVID-19 pandemic, updated appendices.	11.23.20	02.21
2Q 2021 annual review: added criteria for new indication of DIRA for Kineret; added additional criteria related to diagnosis of PsO per 2019 AAD/NPF guidelines specifying involvement of areas that severely impact daily function OR at least 3% BSA involvement for moderate-to-severe, at least 10% BSA involvement for chronic-severe; added biosimilar redirection to other diagnoses/indications; added alopecia areata as indication not coverable for Xeljanz/Xeljanz XR requests (cosmetic); updated CDAI table with ">" to prevent overlap in classification of severity; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); clarified that different therapeutic classes must be tried for HS, each for 3 months; references reviewed and updated. RT4: updated criteria to reflect pediatric extension for UC to include patients 5 years of age and older. RT4: added criteria for new FDA indication, SSc-ILD	05.04.21	05.21
RT4: updated Cosentyx PsO age requirement from ≥ 18 years to ≥ 6 years per FDA pediatric expansion; added new 75 mg/0.5 mL prefilled syringe for pediatric patients. RT4: added new Skyrizi 150 mg/mL prefilled pen and syringe formulations.	06.04.21	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and

accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.