DRUG DETERMINATION POLICY

Title: DDP-11 Interleukin Inhibitors

Effective Date: 03/25/2021

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs that require prior approval.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Preferred Interleukin Inhibitors are specialty drugs indicated for a number of diagnoses and are associated with significant toxicity. These medications include, but are not limited to: Actemra (tocilizumab), Cosentyx (secukinumab), Stelara (ustekinumab), Tremfya (guselkumab), and Skyrizi (risankizumab). (Other interleukin inhibitors not covered on formulary include Ilumya, Taltz, Siliq, and Kevzara.) These criteria for prior approval (PA) were developed and implemented to ensure appropriate use for the intended diagnoses and mitigation of toxicity, if possible.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. Inflammatory bowel disease (IBD) [must meet all l listed below]:

   A. Age: at least 12 years.

   B. Diagnosis and severity: moderate to severe active Crohn's disease or ulcerative colitis.

   C. Other therapies: contraindicated, inadequate response after four months of each agent or significant adverse effects to one conventional therapy and one disease modifying anti-rheumatic drug (DMARDs) below:

      1. Conventional therapies: mesalamine.

      2. Chronic traditional disease-modifying anti-rheumatic drug (DMARD): azathioprine, methotrexate.

3. Exceptions: skipping the requirements of "*2. Other therapies"* are allowed if patient exhibits severe or fulminant disease (see Appendix I) or has ileal Cohn's disease.

D. Dosage regimen: Stelara intravenous and subcutaneous (ustekinumab IV, SQ):

AGE	LOADING DOSE IV	MAINTENANCE DOSE SQ
Adult and Pediatric	< 55Kg: 260mg ≥ 55Kg - 85Kg: 390mg > 85Kg: 520mg	90mg every 8 weeks

E. Approval.

1. Initial: six months.

2. Re-approval: one year.

II. Rheumatology.

A. Rheumatoid Arthritis [must meet all listed below]:

1. Age: at least 18 years.

2. Diagnosis and severity: moderate to severe rheumatoid arthritis.

3. Other therapies: contraindicated, inadequate response after four months of each agent or significant adverse events with two therapies:

a. Chronic traditional DMARD: leflunomide, methotrexate, hydroxychloroquine, sulfasalazine.

4. Dosage regimen.

a. Actemra intravenous (tocilzumab IV): 4mg per Kg every four weeks; increase to 8mg per Kg with inadequate response (maximum 800mg).

5. Exclude: Actemra subcutaneous (tocilzumab SQ) and Kevzara subcutaneous (sarilumab SQ).

a. Contraindicated, inadequate response or significant adverse effects to all preferred products.

b. Requires site of care determined by the Health Plan (see DDP-08 Site of Care for Administration of Parenteral Specialty Medications).

B. Psoriatic Arthritis [must meet all listed below]:

1. Age: at least 18 years.

2. Diagnosis and severity: active PA with at least five swollen and at least five tender joints.

3. Other therapies: contraindicated, inadequate response after four months of each agent or to significant adverse effects from two from the appropriate category below:

a. Peripheral disease: chronic traditional disease modifying antirheumatic drug (DMARD) therapy (four months) - methotrexate, leflunomide, sulfasalazine.

b. Axial disease, enthesitis, dactylitis and uveitis: nonsteroidal anti-inflammatory drugs (NSAIDs) (four months).

4. Excluded: Taltz subcutaneous (ixekizumab SQ).

a. Contraindicated, inadequate response after four months or significant adverse effects to all preferred products.

5. Dosage regimen:

a. Cosentyx subcutaneous (secukinumab SQ): 300mg weekly times five, then 150mg every four weeks (may increase to 300mg if inadequate response).

b. Stelara subcutaneous (ustekinumab SQ):

- Standard: 45mg week zero and four, then 45mg every twelve weeks.

- Co-morbid moderate to severe plaque psoriasis (over100kg): 90 mg week zero and four, then 90mg every twelve weeks.

c. Tremfya subcutaneous (guselkumab SQ): 100mg weeks zero, four, and then every eight weeks thereafter.

6. Approval:

a. Initial: six months.

b. Re-approval: one year (decreased or sustained reduction in disease activity, as shown by less joints affected).

C. Ankylosing Spondylitis [must meet all listed below]:

1. Age: at least 18 years.

2. Diagnosis and severity: active ankylosing spondylitis.

3. Other therapies: contraindicated, inadequate response after four months of each agent or significant adverse effects (two DMARDs below):

a. Chronic traditional DMARD: methotrexate, leflunomide, sulfasalazine.

4. Dosage regimen:

a. Cosentyx subcutaneous (secukinumab SQ): 150mg weekly times five, then 150mg every four weeks.

5. Approval.

a. Initial: six months.

b. Re-approval: one year (decreased or sustained reduction in disease activity, as shown by less joints affected).

D. Axial Spondyloarthritis (non-radiographic) [must meet all listed below]:

1. Age: at least 18 years.

2. Diagnosis and severity.

   a. Active Axial Spondyloarthritis with objective signs of inflammation.

   b. Severity: C-reactive protein (CRP) level above the upper limit of normal and/or evidence of sacroilitis on Magnetic Resonance Imaging (MRI).

3. Other therapies: contraindicated, inadequate response after four months of each agent or significant adverse effects.

   a. Chronic traditional DMARD: methotrexate, leflunomide, sulfasalazine.

4. Dosage regimen.

   a. Cosentyx subcutaneous (secukinumab SQ): 150mg weekly times five, then 150mg every four weeks.

5. Approval.

   a. Initial: six months.

   b. Re-approval: one year (decreased or sustained reduction in disease activity, as shown by less joints affected).

E. Polyarticular Juvenile idiopathic arthritis [must meet all listed below]:

1. Age: at least two years.

2. Diagnosis and severity: moderate to severe active Juvenile Idiopathic Arthritis.

3. Other therapies: contraindication, inadequate response after four months of each agent or significant adverse effects to two DMARD therapies.

   a. Chronic traditional DMARDs: methotrexate, leflunomide, anakinra.

4. Dosage regimen: Actemra Intravenous (tocilizumab IV).

WEIGHT	DOSE	FREQUENCY
<30Kg	10mg/Kg	4weeks
≥30Kg	8mg/Kg	4 weeks

III. Dermatology.

A. Plaque Psoriasis [must meet all listed below]:

1. Age: at least six years.

2. Diagnosis and severity: moderate to severe chronic plaque psoriasis.

a. Duration: chronic plaque psoriasis greater than six months.

b. Severity [must meet one listed below]:

- Body Surface area (BSA): at least 10% OR

- Severe at localized sites and associated with significant functional impairment (e.g., involvement of high-impact and difficult to treat sites such as the face, palms, soles, flexures and genitals).

3. Other therapies: contraindicated, inadequate response after four months of each agent or significant adverse effects to two local therapies and one of systemic therapies below:

   a. Local therapies: topical (steroids, vitamin D analogues, coal tar, dithranol), phototherapy, photochemotherapy.

   b. Systemic therapy: cyclosporine, methotrexate.

4. Excluded: Taltz subcutaneous (ixekizumab SQ), Siliq subcutaneous (brodalumab SQ) and Ilumya subcutaneous (tildrakizumab SQ).

   a. Contraindicated, inadequate response after four months or significant adverse effects to all preferred products.

5. Dosing regimen:

   a. Cosentyx subcutaneous (secukinumab SQ): 300mg weekly times five, then 150mg every four weeks (may increase to 300mg if inadequate response).

   b. Stelara subcutaneous (ustekinumab SQ):

AGE	LOADING DOSE IV	MAINTENANCE DOSE SQ
Adult	$\leq$ 100Kg: 45mg week 0 and 4 >100Kg: 90mg week 0 and 4	$\leq$ 100Kg: 45mg every 12 weeks >100Kg: 90mg every 12 weeks
Pediatric	< 60 Kg: 0.75mg/Kg week 0 and 4 $\geq$ 60Kg to $\leq$100Kg: 45mg week 0 and 4 >100Kg: 90mg week 0 and 4	0.75mg/Kg every 12 weeks 45mg every 12 weeks 90mg every 12 weeks

   c. Skyrizi (risankizumab): 150mg at weeks zero, four, and then every twelve weeks thereafter.

   d. Tremfya subcutaneous (guselkumab SQ): 100mg weeks zero, four, and then every eight weeks thereafter.

6. Approval:

   a. Initial: six months.

b. Re-approval: one year (decreased or sustained reduction in disease activity, as shown by less joints affected).

IV. Appropriate medication use [must meet one listed below]:

A. FDA approval status [must meet one listed below]:

1. FDA approved: product, indication, and/or dosage regimen.

2. Off-label use: at least two supporting studies from major peer-reviewed medical journals that support the off-label use as safe and effective.

B. Place in therapy: sequence of therapy supported by national or international accepted guidelines and/or studies.

4.0 Coding:

AFFECTED CODES				
Code	**Brand Name**	**Generic Name**	**Billing Units (Iu)**	**Prior approval**
J3357 J3358	Stelara	Ustekinumab	1mg	Y
J3262	Actemra IV	Tocilizumab	1mg	Y
0078-0069-98	Cosentyx 2-pack syringe	Secukinumab	NA	Y
NA	Skyrizi	risankizumab	NA	Y
NA	Tremfya SC	guselkumab	N/A	Y

NON-COVERED CODES		
Code	**Brand Name**	**Generic Name**
J3262	Actemra SC	tocilizumab
NA	Kevzara SC	sarilumab
NA	Siliq SC	brodalumab
NA	Taltz SC	ixekizumab
NA	Ilumya SC	tidrakizumab

5.0 References, Citations & Resources:

1. Lexicomp Online® , Lexi-Drugs® , Hudson, Ohio: Lexi-Comp, Inc.; Cosentyx, Stelara, Actemra, Skyrizi accessed June 2020.
2. Secukinumab in Plaque Psoriasis – results of two phase 3 trials. NEJM 2014; 371:326-338.
3. Ustekinumab induction and maintenance therapy in refractory Crohn's disease. NEJM 2012;367:1519-1528.
4. Comparison of ustekinumab and etanercept for moderate-to-severe psoriasis. NEJM 2010; 362(2):118-28.
5. Ustekinumab inhibits radiographic progression in patients with active psoriatic arthritis: results from the phase 3 PSUMMIT-1 and PSUMMIT-2 trials. Ann Rheum Dis. 2014;73(6):1000-6.
6. 3rd European evidence-based consensus on the diagnosis and management of Crohn's disease 2016: Part 1: Diagnosis and medical management. Journal of Crohn's and Colitis. 2017;11:3-25.
7. British Association of Dermatologists guidelines for the biological therapy for psoriasis 2017;177(3):628-36.
8. Clinical Practice Guidelines for the treatment of patients with axial spondyloarthritis and psoriatic arthritis. Madrid, (Spain): Spanish Society of Rheumatology (SER);2015.

6.0 Appendices:

See pages 8-10.

7.0 Revision History:

Original Effective Date: June 24, 2015

Next Review Date:

Revision Date	Reason for Revision
4/19	Moving to new format
7/19	Opened for annual review by P&T Committee; abbreviations replaced
9/19	Added Skyrizi, Deleted prescriber
2/20	Off cycle review; Tremfya added to formulary, added Appendix I, added Stelara UC indication and additional J code
6/20	Annual review; replaced abbreviation, added diagnosis of Axial Spondyloarthritis (non-radiographic), and juvenile idiopathic arthritis, clarified language/instruction for other therapies and exclusions, added Stelara Pediatric dosing, approved by P&T Committee 8/26/20.
2/21	Off cycle review, added Tremfya to PA diagnosis, Removed scalp from severity of PP, clarified criteria instructions, added appropriate use section

Appendix I - International Definitions of Disease Activity

Supplementary Table 1. International Definitions of Disease Activity in Crohn's Disease and Ulcerative Colitis

Crohn's disease (international definitions based on CDAI parameters[1])

ACG[2]	**Symptomatic remission** CDAI <150 Asymptomatic/without symptomatic inflammatory sequelae May have responded to medical or surgical therapy and have no residual active disease Does not include patients who require corticosteroids	**Mild–moderate** CDAI 150–220 Ambulatory Able to tolerate oral alimentation without manifestations of dehydration, systemic toxicity (high fevers, rigors, and prostration), abdominal tenderness, painful mass, intestinal obstruction, or >10% weight loss	**Moderate–severe** CDAI 220–450 Failed to respond to treatment for mild–moderate disease *or* Has more prominent symptoms of fever, significant weight loss, abdominal pain or tenderness, intermittent nausea or vomiting (without obstructive findings), or significant anemia	**Severe/fulminant** CDAI >450 Persistent symptoms despite treatment with corticosteroids/biologics as outpatients *or* Has high fevers, persistent vomiting, intestinal obstruction, significant peritoneal signs, cachexia, or abscess
ECCO[3]	**Symptomatic remission** CDAI <150	**Mild** CDAI 150–220 Ambulatory Eating and drinking <10% weight loss No obstruction, fever, dehydration, abdominal mass, or tenderness CRP increased above ULN	**Moderate** CDAI 220–450 Intermittent vomiting or weight loss >10% Treatment for mild disease ineffective or tender mass No overt obstruction CRP increased above ULN	**Severe** CDAI >450 Cachexia or evidence of obstruction/abscess Persistent symptoms despite intensive treatment CRP increased

Ulcerative colitis (international definitions based on Truelove–Witts criteria[4])

ACG[5]	**Symptomatic remission**	**Mild** <4 stools/d (with or without blood) No systemic signs of toxicity Normal ESR	**Moderate** ≥4 stools/d Minimal signs of toxicity	**Severe** ≥6 bloody stools/d Signs of toxicity (fever, tachycardia, anemia) Increased ESR	**Fulminant** ≥10 stools/d Continuous bleeding Toxicity Abdominal tenderness and distension Blood transfusion requirement Colonic dilation on abdominal plain films
ECCO[6]	**Symptomatic remission** <4 stools/d without bleeding or urgency	**Mild** <4 bloody stools/d Pulse <90 bmp Temperature <37.5°C Hemoglobin >11.5 g/dL ESR <20 mm/h or normal CRP	**Moderate**[a] ≥4 bloody stools/d *if* Pulse ≤90 bmp Temperature ≤37.8°C Hemoglobin ≥10.5 g/dL ESR ≤30 mm/h or CRP ≤30 mg/dL	**Severe**[b] ≥6 bloody stools/d *and* Pulse >90 bmp Temperature >37.8°C Hemoglobin <10.5 g/dL ESR >30 mm/h or CRP >30 mg/dL	

Appendix II: FDA Approved Indications

FDA Approved Indications	Ulcerative Colitis (UC	Crohn's Disease (CD)	Plaque Psoriasis (PP)	Rheumatoid Arthritis (RA)	Psoriatic Arthritis (PA)	Ankylosing Spondylitis (AS)
Preferred Interleukin Inhibitors						
Actemra IV				X		
Cosentyx SC			X		X	X
Stelara IV/SC	X	X	X		X	
Skyrizi SC			X			
Tremfya SC			X			
Excluded Interleukin Inhibitors						
Actemra SC				X		
Kevzara SC				X		
Siliq SC			X			
Taltz SC			X		X	
Ilumya SC			X			

Appendix III: Monitoring & Patient Safety

Drug	Adverse Reactions	Monitoring	REMS
Stelara Ustekinumab IV/SC	• Central Nervous System (CNS): headache (HA) (5%) • Respiratory: naso-pharyngitis (27-72%) • Other: antibody development (6%) • Pregnancy Risk Factor: B	• Infection: TB Test prior to treatment; watch for signs and symptoms • Miscellaneous: signs and symptoms of skin cancer (CA) (especially with elderly), long therapy, history of PUVA ultraviolet light treatment	• Medication. guide must be dispensed with med
Cosentyx secukinumab	• Infection: nasopharyngitis, candida, herpes, staph skin (29-48%) • Pregnancy Risk Factor: B	• Gastrointestinal (GI): Crohn's flare (0.09%) • Infections: tuberculosis (TB) test - pre-treatment; watch for signs and symptoms	• Med. guide must be dispensed with med
Actemra Tocilizumab IV/SC	• Endocrine/metabolic: ↑ cholesterol (19-20%) • Hepatic: ↑ alanine aminotransferase (ALT) (≤34%); ↑ aspartate aminotransferase (AST) (≤22%) • Miscellaneous: infusion related Rx (4-16%) • Pregnancy: adverse events observed in some animal studies	• CNS: signs and symptoms of demyelinating disorder • GI: perforation • Infections: TB test - pre-treatment • Labs: ALT/AST - pre, 4-8 weeks during, then every 3 months; lipids - pre, 4-8 weeks during, then every 6 weeks)	• Med. guide must be dispensed with med
Skyrizi risankizumab	• Immunologic: antibody development (24%) • Infections: infection (22%) • Respiratory: upper respiratory infection (URI) (13%)	• Infections: TB test – prior and intermittently; signs and symptoms	• None needed