DRUG DETERMINATION POLICY

Title: DDP-11 Interleukin Inhibitors

Effective Date: 8/23/23

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. General considerations for use

A. Appropriate medication use [must meet all listed below]:

1. Diagnosis: meets standard diagnostic criteria that designate signs, symptoms, and test results to support specific diagnosis.

2. Food and Drug Administration (FDA) approval status [must meet one listed below]:

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

b. Non-FDA approved use: Compendium support (Lexicomp®) for use of a drug for a non-FDA approved indication or dosage regimen.

3. Place in therapy: sequence of therapy supported by national or internationally accepted guidelines and/or studies (e.g., oncologic, infectious conditions).

B. Grandfather status: patients currently on excluded interleukin inhibitors may continue therapy.

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

1. Exception: Skyrizi IV (risankizumab)

D. Dose Rounding: medication requests may be automatically rounded up or down by 10% of the requested dose in order to fit the nearest manufacturers strength of the requested medication for patients weighing above 10 Kg (see DDP-21 Dose Rounding and Wastage).

E. Pharmaceutical sample use: The Plan does not recognize samples as a medication trial or for continuation of therapy.

F. Excluded agents: Actemra subcutaneous (tocilizumab SC), Kevzara subcutaneous (sarilumab SC), Siliq subcutaneous (brodalumab SC), Taltz subcutaneous (ixekizumab SC), Ilumya subcutaneous (tidrakizumab SC).

1. Trial of all preferred formulary agents is required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or severe adverse reaction.

G. Exclusion: Concomitant therapy with other biologics.

H. Approval.

1. Initial: six months.

2. Re-approval: one year [must meet both listed below]:

a. Decreased or sustained reduction in disease activity.

b. Adherence [must meet one listed below]:

i. Medications processed on the medical benefit: consistent utilization (at least 80% of days covered) history documented in claims history or chart notes.

ii. Medications processed on the pharmacy benefit: consistent (at least 80% of days covered) fill history electronically or verbally from pharmacy.

II. Inflammatory bowel disease [must meet all listed below]:

A. Crohn's Disease

1. Age: at least 12 years.

2. Diagnosis and severity: moderate to severe active Crohn's disease.

3. Other therapies: Trial of one disease-modifying anti-rheumatic drug below is required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or severe adverse reaction.

a. Chronic traditional disease-modifying anti-rheumatic drug: azathioprine, methotrexate.

b. Exceptions: skipping the requirements of "3. *Other therapies"* are allowed if patient exhibits severe or fulminant disease (see Appendix I).

4. Dosage regimen

a. Stelara intravenous and subcutaneous (ustekinumab IV, SQ):

Age	Loading Dose IV	Maintenance dose SQ
Adult and Pediatric, ≥ 12 years	< 55 kg: 260 mg ≥ 55 kg – 85 kg: 390 mg > 85 kg: 520 mg	90 mg every eight weeks

b. Skyrizi intravenous and subcutaneous (risankizumab IV, SQ):

Age	Loading Dose IV	Maintenance Dose SQ
Adult	600 mg at weeks zero, four, and eight.	360 mg at week twelve and every eight weeks thereafter

B. Ulcerative Colitis

1. Age: at least 12 years.

2. Diagnosis and severity: moderate to severe active Ulcerative Colitis.

3. Other therapies: Trials of one conventional therapy and one disease-modifying anti-rheumatic drug below are required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or severe adverse reaction.

a. Conventional therapy: mesalamine.

b. Chronic traditional disease-modifying anti-rheumatic drug: azathioprine.

c. Exceptions: skipping the requirements of "*3 Other therapies"* are allowed if patient exhibits severe or fulminant disease (see Appendix I).

4. Dosage regimen

a. Stelara intravenous and subcutaneous (ustekinumab IV, SQ):

Age	Loading Dose IV	Maintenance Dose SQ
Adult and pediatric, ≥ 12 years	< 55 Kg: 260 mg ≥ 55 Kg – 85 Kg: 390 mg > 85 Kg: 520 mg	90 mg every 8 weeks

III. 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: Trials of two disease-modifying anti-rheumatic drug below are required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or severe adverse reaction.

    a. Disease modifying anti-rheumatic drugs: leflunomide, methotrexate, hydroxychloroquine, sulfasalazine.

4. Dosage regimen.

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

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

1. Age:

    a. Cosentyx subcutaneous (secukinumab SQ): at least two years.

    b. Skyrizi subcutaneous (risankizumab SQ): at least 18 years.

    c. Stelara subcutaneous (ustekinumab SQ): at least six years.

    d. Tremfya subcutaneous (guselkumab SQ): at least 18 years.

2. Diagnosis and severity: active Psoriatic Arthritis

3. Other therapies: Trials of two from the appropriate category below are required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or severe adverse reaction.

    a. Peripheral disease: chronic traditional disease modifying antirheumatic drug: methotrexate, leflunomide, sulfasalazine.

    b. Axial disease, enthesitis, dactylitis and uveitis: nonsteroidal anti-inflammatory drugs.

4. Dosage regimen:

    a. Cosentyx subcutaneous (secukinumab SQ):

Age	Weight	Loading Doses	Maintenance Dose
Adult	NA	150 mg weekly x five doses	150 mg every four weeks (May increase to 300mg if inadequate response).
Adult with coexistent moderate to severe plaque	NA	300 mg weekly x five doses	300 mg every four weeks

psoriasis			
Pediatric, ≥ 2 years	15 - 49 kg	75 mg weekly x five doses	75 mg every four weeks
	≥50 kg	150 mg weekly x five doses	150 mg every 4 weeks

b. Stelara subcutaneous (ustekinumab SQ):

Age	Weight	Loading Doses	Maintenance Dose
Adult	NA	45 mg at weeks zero and four	45 mg every twelve weeks
Adult with coexistent moderate to severe plaque psoriasis	> 100 kg	90 mg at weeks zero and four	90 mg every twelve weeks
Pediatric, ≥ 6 years	< 60 kg	0.75 mg per kg weeks zero and four	0.75 mg per kg every twelve weeks
	≥ 60 kg	45 mg weeks zero and four	45 mg every twelve weeks

c. Tremfya subcutaneous (guselkumab SQ):

i. Adults only, 18 years and older: 100mg weeks zero, four, and then every eight weeks.

d. Skyrizi subcutaneous (risankizumab SQ):

i. Adults only, 18 years and older: 150mg week zero, four then every twelve weeks.

C. Axial spondyloarthritis (ankylosing spondylitis and nonradiographic axial spondyloarthritis) [must meet all listed below]:

1. Age: at least 18 years.

2. Diagnosis and severity: active ankylosing spondylitis or nonradiographic axial spondyloarthritis

3. Other therapies: Trials of two non-steroidal anti-inflammatory drugs and one disease-modifying anti-rheumatic drug listed below are required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or severe adverse reaction:

a. Non-steroidal anti-inflammatory Agents: prescription agents (e.g., meloxicam, celecoxib, nabumetone)

b. Peripheral dominant disease only: First line disease modifying anti-rheumatic drugs: methotrexate, sulfasalazine.

4. Dosage regimen:

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

        i. Ankylosing spondylitis: may increase to 300 mg every four weeks if inadequate response.

D. Polyarticular and systemic 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: Trials of two disease-modifying anti-rheumatic drugs below are required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or severe adverse reaction.

    a. Disease modifying anti-rheumatic drugs: methotrexate, leflunomide.

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

Weight	Dose	Frequency
< 30 kg	10 mg per kg	Every four weeks
≥ 30 kg	8 mg per kg, maximum of 800 mg per dose	Every four weeks

IV. 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]:

        i. Body Surface area: at least 10%

        ii. 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: Trials of two local therapies and one of systemic therapy below are required unless all are contraindicated. Trial must result in an inadequate response after four consecutive months of use per medication or severe adverse reaction.

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

b. Systemic therapy: cyclosporine, methotrexate.

4. 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	Weight	Loading Doses	Maintenance Dose
Adults	≤ 100 kg	45 mg at weeks zero and four	45 mg every twelve weeks
	> 100 kg	90 mg at weeks zero and four	90 mg every twelve weeks
Pediatric, ≥ 6 years	< 60 kg	0.75 mg per kg weeks zero and four	0.75 mg per kg every twelve weeks
	≥ 60 kg	45 mg weeks zero and four	45 mg every twelve weeks

c. Skyrizi (risankizumab):

i. Adults only, 18 years and older:150mg at weeks zero, four, and then every twelve weeks thereafter.

d. Tremfya subcutaneous (guselkumab SQ):

i. Adults only, 18 years and older: 100mg weeks zero, four, and then every eight weeks thereafter.

4.0 Coding:

COVERED CODES - MEDICAL BENEFIT				
HCPCS Code	**Brand Name**	**Generic Name**	**Billing (1 Unit)**	**Prior Approval**
J3358	Stelara IV	ustekinumab	1mg	Y
J3262	Actemra IV	tocilizumab	1mg	Y
J2327	Skyrizi IV	risankizumab	1mg	Y

COVERED PRODUCTS - PHARMACY BENEFIT			
NDC	**Brand Name**	**Generic Name**	**Prior Approval**
00078-1056-97	Cosentyx SC (1-pack of 75mg prefilled syringes)	secukinumab	Y
00078-0639-41	Cosentyx SC (2-pack of 150 mg Sensoready Pens)	secukinumab	Y
0078-0069-98	Cosentyx SC (2-pack of 150 mg prefilled syringes)	secukinumab	Y
All	Stelara SC	ustekinumab	Y
All	Skyrizi SC	risankizumab	Y
All	Tremfya SC	guselkumab	Y

EXCLUDED CODES AND PRODUCTS			
HCPCS Code	**Brand Name**	**Generic Name**	**Benefit Plan Reference/Reason**
J1628	Tremfya SC	guselkumab	Covered on the pharmacy benefit with prior approval
J3245	Ilumya SC	tidrakizumab	Not a Preferred agent
J3262	Actemra SC	tocilizumab	Not a Preferred agent
J3357	Stelara SC	ustekinumab	Covered on the pharmacy benefit with prior approval
NA	Kevzara SC	sarilumab	Not a Preferred agent
NA	Siliq SC	brodalumab	Not a Preferred agent
NA	Taltz SC	ixekizumab	Not a Preferred agent

5.0 References, Citations & Resources:

1. Lexi comp Online®, Lexi-Drugs® , Hudson, Ohio: Lexi-Comp, Inc.; Cosentyx, Stelara, Actemra, Skyrizi, Tremfya accessed June 2022.
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: 06/24/2015

Next Review Date: 08/24/2023

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
6/21	Annual review, reformatted, clarified instructions, added compendium for non-FDA approved use
2/22	Annual review requested to open early; added Skyrizi for psoriatic arthritis, updated indication table, added to FDA approved (including newly approved indications not listed above); removed highlighting from changes
4/22	Off-cycle review requested by Ann Hunt Fugate, formatting change; separated other therapies for CD and UC removed MTX for UC and mesalamine for CD Combine sections for ankylosing spondylitis and nonradiographic axial spondyloarthritis and clarified other therapies;
6/23	Annual review: Added general considerations for use section, clarified “other therapies” language, updated coding, updated FDA indications table, moved excluded drugs to general considerations for 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	Inflamma-tory Bowel Disease (CD, UC)	Plaque Psoriasis	Juvenile idiopathic arthritis	Rheum-atoid Arthritis	Psoriatic Arthritis	Axial Spondylo-arthritis (AS, NSpA)	Giant Cell Arteritis	Inter-stitial Lung Disease	Cytokine Release syndrome
Preferred Interleukin Inhibitors									
Actemra IV			X (P)	X			X	X	X (P)
Cosentyx SC		X (P)			X (P)	X			
Stelara IV/SC	X	X (P)			X (P)				
Skyrizi SC	X (CD)	X			X				
Tremfya SC		X			X				
Excluded Interleukin Inhibitors									
Actemra SC			X (P)	X			X	X	
Kevzara SC				X					
Siliq SC		X							
Taltz SC		X (P)			X	X			
Ilumya SC		X							

AS: ankylosing spondylitis, CD: Crohn's Disease, P: Pediatric indication, NSpA: nonradiographic axial spondyloarthritis, UC: Ulcerative Colitis

Appendix III: Monitoring & Patient Safety

Drug	Adverse Reactions	Monitoring	REMS
Stelara Ustekinumab IV/SC	• Central Nervous System (CNS): headache (HA) (5%) • Respiratory: nasopharyngitis (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 drug
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	• Medication guide must be dispensed with drug
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)	• Medication guide must be dispensed with drug
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