Targeted Immune Modulators for Autoimmune Conditions

Goal(s):

- Promote use that is consistent with national clinical practice guidelines and medical evidence.
- Restrict use of targeted immune modulators to OHP-funded diagnoses in adults.
- Allow case-by-case review for members covered under the EPSDT program.
- Promote use of cost-effective products.

Length of Authorization:

- Up to 12 months

Requires PA:

- All targeted immune modulators for autoimmune conditions (both pharmacy and physician-administered claims)

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Table 1. Targeted Immune Modulators FDA-Approved for Ankylosing Spondylitis, Juvenile Idiopathic Arthritis, Rheumatoid Arthritis, and Non-Radiographic Axial Spondyloarthritis

Generic Name (BRAND NAME)	Ankylosing Spondylitis (AS)	Juvenile Idiopathic Arthritis (JIA)	Rheumatoid Arthritis (RA)	Non-Radiographic Axial Spondyloarthritis (NR-axSpA)
Tier 1 (Preferred First-Line)				
Adalimumab (HUMIRA)	≥18 y	≥2 yo	≥18 yo	
Adalimumab-atto (AMJEVITA)	≥18 y	≥2 yo	≥18 yo	
Adalimumab-fkjp 50 mg/mL	≥18 y	≥2 yo	≥18 yo	
Adalimumab-ryvk (SIMLANDI)	≥18 y	≥2 yo	≥18 yo	
Etanercept (ENBREL)	≥18 yo	≥2 yo	≥18 yo	
Infliximab-axxq (AVSOLA)	≥18 yo		≥18 yo	
Tier 2 (Preferred Second-Line)				
Ixekizumab (TALTZ)	≥ 18 yo			≥18 yo
Tofacitinib (XELJANZ)	≥18 yo	≥2 yo	≥18 yo	
Tier 3 (Non-Preferred Third-Line)				
Abatacept (ORENCIA)		≥2 yo	≥18 yo	
Anakinra (KINERET)			≥18 yo	
Baricitinib (OLUMIANT)			≥18 yo	
Bimekizumab (BIMZELX)	≥18 yo			≥18 yo
Canakinumab (ILARIS)		≥2 yo		
Certolizumab (CIMZIA)	≥18 yo	≥2 yo	≥18 yo	≥18 yo
Golimumab (SIMPONI and SIMPONI ARIA)	≥18 yo	≥2 yo (SIMPONI ARIA)	≥18 yo	
Infliximab (REMICADE)	≥18 yo		≥18 yo	
Rituximab (RITUXAN)			≥18 yo	
Sarilumab (KEVZARA)			≥18 yo	
Secukinumab (COSENTYX)	≥18 yo			≥18 yo
Tocilizumab (ACTEMRA)		≥2 yo	≥18 yo	
Upadacitinib (RINVOQ)	≥18 yo	≥2 yo	≥18 yo	≥18 yo

Note: Biosimilar products are Tier 3 unless specifically mentioned

Table 2. Targeted Immune Modulators FDA-Approved for Plaque Psoriasis, Psoriatic Arthritis, and Hidradenitis Suppurativa

Generic Name (BRAND NAME)	Plaque Psoriasis (PsO)	Psoriatic Arthritis (PsA)	Hidradenitis Suppurativa (HS)
Tier 1 (Preferred First-Line)			
Adalimumab (HUMIRA)	≥18 yo	≥18 yo	≥ 12 yo
Adalimumab-atto (AMJEVITA)	≥18 yo	≥18 yo	≥18 yo
Adalimumab-fkjp 50 mg/mL	≥18 yo	≥18 yo	
Adalimumab-ryvk (SIMLANDI)	≥18 yo	≥18 yo	≥18 yo
Etanercept (ENBREL)	≥4 yo	≥2 yo	
Infliximab-axxq (AVSOLA)	≥18 yo	≥18 yo	
Tier 2 (Preferred Second-Line)			
Ixekizumab (TALTZ)	≥6 yo	≥18 yo	
Tofacitinib (XELJANZ)		≥18 yo	
Tier 3 (Non-Preferred Third-Line)			
Abatacept (ORENCIA)		≥2 yo	
Apremilast (OTEZLA)	≥ 6 yo and weighing ≥ 20 kg	≥18 yo	
Bimekizumab (BIMZELX)	≥18 yo	≥18 yo	≥18 yo
Brodalumab (SILIQ)	≥18 yo		
Certolizumab (CIMZIA)	≥18 yo	≥18 yo	
Deucravacitinib (SOTYKU)	≥18 yo		
Golimumab (SIMPONI and SIMPONI ARIA)		≥2 yo (SIMPONI ARIA) ≥18 yo (SIMPONI)	
Guselkumab (TREMFYA)	≥18 yo	≥18 yo	
Infliximab (REMICADE)	≥18 yo	≥18 yo	
Risankizumab (SKYRIZI)	≥18 yo	≥18 yo	
Secukinumab (COSENTYX)	≥6 yo	≥2 yo	≥18 yo
Tildrakizumab (ILUMYA)	≥18 yo		
Upadacitinib (RINVOQ)		≥2 yo	
Ustekinumab (STELARA)	≥6 yo	≥6 yo	

Note: Biosimilar products are Tier 3 unless specifically mentioned

Table 3. Targeted Immune Modulators FDA-Approved for Crohn's Disease and Ulcerative Colitis

Generic Drug Name (BRAND NAME)	Crohn's Disease	Ulcerative Colitis
Tier 1 (Preferred First-Line)		
Adalimumab (HUMIRA)	≥6 yo	≥5 yo
Adalimumab-atto (AMJEVITA)	≥6 yo	≥18 yo
Adalimumab-fkjp 50 mg/mL	≥6 yo	≥18 yo
Adalimumab-ryvk (SIMLANDI)	≥6 yo	≥18 yo
Infliximab-axxq (AVSOLA)	≥6 yo	≥6 yo
Tier 2 (Preferred Second-Line)		
Tofacitinib (XELJANZ)		≥18 yo
Tier 3 (Non-Preferred Third-Line)		
Certolizumab (CIMZIA)	≥18 yo	
Etrasimod (VELSIPITY)		≥18 yo
Golimumab (SIMPONI and SIMPONI ARIA)		≥18 yo (SIMPONI)
Guselkumab (TREMFYA)		≥18 yo
Infliximab (REMICADE)	≥6 yo	≥6 yo
Mirikizumab (OMVOH)		≥18 yo
Risankizumab (SKYRIZI)	≥18 yo	≥18 yo
Ozanimod (ZEPOSIA)		≥18 yo
Upadacitinib (RINVOQ)	≥ 18 yo	≥18 yo
Ustekinumab (STELARA)	≥ 18 yo	≥18 yo
Vedolizumab (ENTYVIO)	≥18 yo	≥18 yo

Note: Biosimilar products are Tier 3 unless specifically mentioned

Table 4. Targeted Immune Modulators FDA-Approved for Other Indications not Listed in Table 1, 2 or 3

Generic Drug Name (BRAND NAME)	Other Indications
Adalimumab (HUMIRA) & biosimilars	• Uveitis (non-infectious) ≥2 yo
Abatacept (ORENCIA)	• Acute Graft Versus Host Disease (aGVHD) ≥ 2 yo
Anakinra (KINERET)	• DIRA • COVID ≥ 18 yo (hospitalized) • NOMID
Apremilast (OTEZLA)	• Oral Ulcers associated with Behcet's Disease ≥ 18 yo
Baricitinib (OLUMIANT)	• COVID ≥ 18 yo (hospitalized)
Canakinumab (ILARIS)	• FCAS ≥4 yo • FMF ≥ 4 yo • Gout flares unresponsive to NSAIDs and colchicine ≥18 yo • HIDS ≥ 4 yo • MKD ≥ 4 yo • MWS ≥ 4 yo • Stills Disease ≥ 2 yo • TRAPS ≥ 4 yo
Rituximab (RITUXAN) and biosimilars	• BL ≥ 6 mo • BLL ≥ 6 mo • B-AL ≥ 6 mo • CLL ≥ 18 yo • DLBCL ≥ 6 mo • GPA ≥ 2yo • MPA ≥ 2 yo • NHL ≥18 yo • Pemphigus Vulgaris ≥ 18 yo (RITUXAN only)
Sarilumab (KEVZARA)	• Polymyalgia Rheumatica (PMR) ≥ 18 yo
Secukinumab (COSENTYX)	• Enthesitis-Related Arthritis (ERA) ≥ 4 yo
Spesolimab (Spevigo)	• Generalized Pustular Psoriasis Flares >12 yo and weighing >40 kg • Generalized Pustular Psoriasis after Flares >12 yo and weighing >40 kg
Tocilizumab (ACTEMRA)	• CRS ≥2 yo • COVID ≥ 18 yo (hospitalized) • GCA ≥18 yo • SSc-ILD ≥ 18 yo
Upadacitinib (RINVOQ)	• Atopic Dermatitis ≥ 12 yo

Abbreviations: BL = Burkitt Lymphoma; BLL = Burkitt-like Lymphoma; B-AL = mature B-cell acute leukemia; CLL = Chronic Lymphocytic Leukemia; COVID = Covid-19 infection; CRS = Cytokine Release Syndrome; DIRA = Deficiency of Interleukin-1 Receptor Antagonist; DLBCL = Diffuse Large B-Cell Lymphoma; FCAS = Familial Cold Autoinflammatory Syndrome; FMF = Familial Mediterranean Fever; GCA = Giant Cell Arteritis; GPA = Granulomatosis with Polyangiitis (Wegener's Granulomatosis); HIDS: Hyperimmunoglobulin D Syndrome; MKD = Mevalonate Kinase Deficiency; mo = months old; MPA = Microscopic Polyangiitis; MWS = Muckle-Wells Syndrome; NHL = Non-Hodgkin's Lymphoma; NOMID = Neonatal Onset Multi-Systemic Inflammatory Disease; NSAIDs = non-steroidal anti-inflammatory drugs; SSc-ILD = Systemic Sclerosis-Associated Interstitial Lung Disease; TRAPS = Tumor Necrosis Factor Receptor Associated Periodic Syndrome; yo = years old

Table 5. First-Line Conventional Therapy Recommended for Select Conditions

Conditions	Recommended Conventional Therapy Prior To A Targeted Immune Modulator
Arthritis (Juvenile Idiopathic, Psoriatic, Rheumatoid)	• DMARD therapy: Methotrexate, leflunomide, sulfasalazine or hydroxychloroquine for ≥ 6 months; AND • Concurrent DMARD therapy with plans to continue concomitant use. Biologic therapy is recommended in combination with DMARDs (e.g. methotrexate) for those who have had inadequate response with DMARDs.
Atopic Dermatitis	• Moderate to high potency topical corticosteroid (e.g., clobetasol, desoximetasone, desonide, mometasone, betamethasone, halobetasol, fluticasone, or fluocinonide), in combination with a topical calcineurin inhibitor (e.g., tacrolimus) for at least 4 weeks OR

Conditions	Recommended Conventional Therapy Prior To A Targeted Immune Modulator
	• Oral immunomodulator therapy (e.g., cyclosporine, methotrexate, or azathioprine) for at least 8 weeks
Crohn's Disease	• Mercaptopurine, methotrexate, or azathioprine for ≥6 months
Generalized Pustular Psoriasis	• Acitretin, methotrexate, or cyclosporine for ≥ 3 months
Hidradenitis Suppurativa (HS)	• 90-day trial of conventional HS therapy (e.g. oral antibiotics)
Plaque Psoriasis	• Topical high potency corticosteroid (e.g., betamethasone dipropionate 0.05%, clobetasol propionate 0.05%, fluocinonide 0.05%, halcinonide 0.1%, halobetasol propionate 0.05%; triamcinolone 0.5%) for a minimum of 4 weeks; AND • At least one other topical agent: calcipotriene, tazarotene, anthralin for a minimum of 8 weeks; AND • Phototherapy for at least 8 weeks; AND • At least one other systemic therapy: acitretin, cyclosporine, or methotrexate for at least 16 weeks
Ulcerative Colitis	• 5-aminosalicylate products, mercaptopurine, or azathioprine for ≥6 months
Abbreviations: DMARD=Disease Modifying Anti-Rheumatic Drug; HS=Hidradenitis Suppurativa	

Table 6. FDA-recommended Baseline Safety Tests for Sphingosine 1-Phosphate Receptor Modulators

	Negative Pregnancy Test	LFTs	CBC with lymphocyte count	Ophthalmic Exam	Baseline ECG (see notes)	Skin Exam for Malignancy	Varicella Zoster Antibodies
Etrasimod (VELSIPITY)	X	X	X	X	X	X	X
Ozanimod (ZEPOSIA)	X	X	X	X	X		X
Abbreviations: CBC=complete blood count; ECG=electrocardiogram; FDA =Food and Drug Administration; LFTs = liver function tests							

Sphingosine 1-Phosphate Receptor Modulators Clinical Notes:

- Patients on antiarrhythmics, beta-blockers or calcium channel blockers or with risk factors for bradycardia (h/o MI, age >70 yrs., electrolyte disorder, hypothyroidism) may be more prone to development of symptomatic bradycardia and should be initiated on etrasimod or ozanimod with caution. A cardiology evaluation should be performed before considering treatment in patients with significant QT prolongation, heart disease, heart failure, history of cardiac arrest or myocardial infarction, cerebrovascular disease, and uncontrolled hypertension, a history of with second-degree Mobitz type II or higher AV block, sick-sinus syndrome, or sinoatrial heart block.
- An ophthalmology evaluation should be repeated 3-4 months after etrasimod or ozanimod initiation with subsequent evaluations based on clinical symptoms.

Approval Criteria	
1. What diagnosis is being treated?	Record ICD-10 code.

Approval Criteria		
2. Is the diagnosis funded by OHP? Notes: A. Mild-to-moderate psoriasis, plaque psoriasis, and atopic dermatitis are unfunded, severe forms are funded. B. Mild Hidradenitis Suppurativa (HS) is unfunded, moderate-to-severe HS (e.g., Hurley Stage II or III) is funded. C. Alopecia areata is unfunded. Psoriasis and atopic dermatitis are severe in nature when resulting in functional impairment as indicated by Dermatology Life Quality Index (DLQI) ≥ 11 or Children's DLQI ≥ 13 (or severe score on other validated tool) AND one or more of the following: • At least 10% body surface area involvement; OR • Hand, foot, face, or mucous membrane involvement?	**Yes:** Go to # 4	**No:** If not eligible for EPSDT review: Pass to RPh. Deny; not funded by the OHP. If eligible for EPSDT review: Go to #3.
3. Is there documentation that the condition is of sufficient severity that it impacts the patient's health (e.g., quality of life, function, growth, development, ability to participate in school, perform activities of daily living, etc)?	**Yes:** Go to #4	**No:** Pass to RPh. Deny, medical necessity.
4. Is the request for a drug FDA-approved for this condition and age as defined in Table 1,2,3 or 4 above?	**Yes:** Go to #6	**No:** Go to #5
5. Is there documentation of 1) inadequate response, contraindication or intolerance to FDA-approved targeted immune modulators AND 2) prescribing by, or in consultation with, a relevant specialist for the condition?	**Yes**: Go to #6	**No:** Pass to RPh. Deny; medical appropriateness.

Approval Criteria		
6. Has the patient been annually screened for latent or active tuberculosis and if positive, started tuberculosis treatment? *(Note: this requirement does not apply to requests for apremilast.)	**Yes:** Go to #7	**No:** Pass to RPh. Deny; medical appropriateness. If patient meets all other criteria, may approve once for up to 3 months to allow time for screening for ongoing therapy to avoid interruptions in care.
7. Is this a request for continuation of therapy?	**Yes**: Go to **Renewal Criteria**	**No:** Go to #8
8. Is there documentation of one of the following: • Treatment failure or inadequate response to conventional treatment in outlined Table 5 OR • contraindication or intolerance to first-line conventional treatments outlined in Table 5 OR • request is for a condition not outlined in Table 5?	**Yes:** Go to #9 Document each therapy with dates. If applicable, document intolerance or contraindication(s).	**No**: Pass to RPh. Deny; medical appropriateness
9. Is the request for 1) a preferred Tier 1 product in Table 1, 2 or 3 OR 2) a preferred Tier 2 product if there is no Tier 1 product listed for the indication?	**Yes:** Go to #11	**No:** Go to #10
10. Is there documentation that therapy with an agent from each of the preferred tiers would be inappropriate? <u>Note:</u> documentation could include inadequate response after ≥3 months with at least one product from each preferred tier, contraindication or intolerance to products from each preferred tier, or lack of products FDA-approved for the requested indication in tiers. <u>Message</u>: Preferred products are reviewed for comparative effectiveness and safety by the Oregon Pharmacy and Therapeutics Committee.	**Yes:** Go to #11	**No**: Pass to RPh. Deny; medical appropriateness. Require trial of at least one product from each tier.

Approval Criteria		
11. Is the request for upadacitinib for severe atopic dermatitis?	**Yes:** Go to #12	**No:** Go to #13
12. Has the provider submitted baseline assessment for the severity of atopic dermatitis: Eczema Area and Severity Index score (EASI 50) OR Dermatology Life Quality Index (DLQI) OR Investigators Global Assessment (IGA) score?	**Yes:** Document date of baseline assessment and results here_____ Go to #14	**No:** Pass to RPh. Deny; medical appropriateness
13. Is the request for a JAK inhibitor (e.g., tofacitinib, baricitinib, or upadacitinib)?	**Yes:** Go to #14	**No:** Go to #15
14. Is the patient currently on other biologic therapy or on a potent immunosuppressant like azathioprine, tacrolimus OR cyclosporine? Note: Tofacitinib, baricitinib, and upadacitinib may be used concurrently with methotrexate or other nonbiologic DMARD drugs. Tofacitinib, baricitinib, or upadacitinib are not recommended to be used in combination with other JAK inhibitors, biologic DMARDs, azathioprine, or cyclosporine.	**Yes:** Pass to RPh. Deny; medical appropriateness.	**No:** Approve baricitinib or upadacitinib for up to 6 months. Approve tofacitinib for up to 6 months at a maximum dose of 10 or 11 mg daily for Rheumatoid Arthritis OR 10 mg twice daily for 8 weeks then 5 or 10 mg twice daily for Ulcerative Colitis
15. Is the prescription for a sphingosine 1-phosphate receptor modulator (etrasimod or ozanimod)?	**Yes:** Go to #16	**No:** Go to #19
16. Have baseline safety assessments been completed as outlined in **Table 6**?	**Yes:** Go to #17	**No:** Pass to RPh. Deny; medical appropriateness.
17. Does the patient have preexisting cardiac disease, risk factors for bradycardia, or is on an anti-arrhythmic, beta-blocker, or calcium channel blocker?	**Yes:** Go to #18	**No:** Go to #19
18. Has the patient had a cardiology consultation before initiation (see clinical notes attached to **Table 6**)?	**Yes:** Go to #19	**No:** Pass to RPh. Deny; medical appropriateness.

Approval Criteria	
19. Duration of initial approval based on indication	AS, Plaque psoriasis, RA, AD: 6 months HS: 12 weeks UC/Crohn's: 12 months Other: length of treatment or 1 year, whichever is longer

Renewal Criteria		
1. Is the request to renew therapy for atopic dermatitis?	**Yes:** Go to #2	**No:** Go to #3
2. Have the patient's symptoms improved with upadacitinib therapy? • at least a 50% reduction in the Eczema Area and Severity Index score (EASI 50) from when treatment started, OR • at least a 4-point reduction in the Dermatology Life Quality Index (DLQI) from when treatment started, OR • at least a 2-point improvement on the Investigators Global Assessment (IGA) score?	**Yes:** Approve for 12 months	**No:** Pass to RPh. Deny; medical appropriateness.
3. Is the request for continuation of adalimumab or secukinumab to treat moderate-to-severe Hidradenitis Suppurativa in an adult?	**Yes:** Go to #4	**No:** Go to #5
4. Has the patient had clear evidence of response to adalimumab therapy as evidenced by: • a reduction of 25% or more in the total abscess and inflammatory nodule count, AND • no increase in abscesses and draining fistulas.	**Yes:** Approve for an additional 12 weeks of therapy	**No:** Pass to RPh. Deny; medical appropriateness.
5. Has the patient been adherent to both biologic and DMARD therapy (if DMARD therapy has been prescribed in conjunction with the biologic therapy)?	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness.

Renewal Criteria		
6. Has the patient's condition improved as assessed by the prescribing provider and provider attests to patient's improvement?	**Yes:** Approve for 12 months. Document baseline assessment and provider attestation received.	**No:** Pass to RPh; Deny; medical appropriateness.

P&T/DUR Review: 8/24(DM); 6/23; 10/22; 6/2; 10/21; 10/20; 2/20; 5/19; 1/19; 1/18; 7/17; 11/16; 9/16; 3/16; 7/15; 9/14; 8/12
Implementation: 1/1/25; 9/1/24; 7/1/23; 1/1/23; 7/1/22; 1/1/22; 1/1/2021; 7/1/2019; 3/1/19; 3/1/18; 9/1/17; 1/1/17; 9/27/14; 12/12