Effective Date **6/1/2024**
Coverage Policy Number **IP0231**

Abatacept Subcutaneous

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Related Coverage Resources

Abatacept Intravenous - (IP0232)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for abatacept (**Orencia®**) subcutaneous.

The coverage of abatacept (Orencia) intravenous is addressed in a separate coverage policy, refer to the related coverage policy resources section above (*Abatacept Intravenous - IP0232*).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Abatacept (Orencia) subcutaneous considered medically necessary when ONE of the following is met:

1. **Polyarticular Juvenile Idiopathic Arthritis (includes Juvenile Idiopathic Arthritis [JIA] or Juvenile Rheumatoid Arthritis [JRA]).** Individual meets **BOTH** of the following criteria:
   A. Medication is being prescribed by, or in consultation with, a rheumatologist
   B. Non-Preferred Product Criteria is met, refer to the below table(s) [Employer Group Plans, Individual and Family Plan]

2. **Psoriatic Arthritis.** Individual meets **ALL** of the following criteria:
   A. 18 years of age or older
   B. Documentation of **ONE** of the following:
      i. For Non-axial disease, failure to **ONE** disease-modifying anti-rheumatic drug (DMARD), unless contraindicated or intolerant
      ii. For Axial disease, failure to **ONE** disease-modifying anti-rheumatic drug (DMARD), OR a nonsteroidal anti-inflammatory drug (NSAID), unless contraindicated or intolerant
      iii. Already tried a biologic or targeted synthetic DMARD (tsDMARD) for Psoriatic Arthritis
   C. Medication is being prescribed by, or in consultation with, a rheumatologist or dermatologist
   D. Non-Preferred Product Criteria is met, refer to the below table(s) [Employer Group Plans, Individual and Family Plan]

3. **Rheumatoid Arthritis.** Individual meets **ALL** of the following criteria:
   A. 18 years of age or older
   B. Documentation of **ONE** of the following:
      i. Failure to **ONE** disease-modifying anti-rheumatic drug (DMARD), unless contraindicated or intolerant
      ii. Already tried a biologic or targeted synthetic DMARD for Rheumatoid Arthritis
   C. Medication is being prescribed by, or in consultation with, a rheumatologist
   D. Non-Preferred Product Criteria is met, refer to the below table(s) [Employer Group Plans, Individual and Family Plan]

Coverage varies across plans and may require the use of Preferred Products. Refer to the customer's benefit plan document for coverage details.

Employer Group Plans	
Condition(s)	**Non-Preferred Product Criteria**
Polyarticular Juvenile Idiopathic Arthritis	Documentation of failure, contraindication, or intolerance to **TWO** of the following: A. **Actemra SC** [requires prior authorization] B. **Adalimumab Product: Adalimumab-adaz/Hyrimoz** (by Sandoz/Novartis)**, Adalimumab – adbm/Cyltezo**, **Adalimumab-ryvk/Simlandi,** or **Humira** (by AbbVie) [requires prior authorization] C. **Enbrel** [requires prior authorization] D. **Xeljanz/Xeljanz Oral Solution** [requires prior authorization] A.
Psoriatic Arthritis - Adult	Documentation of failure, contraindication, or intolerance to **TWO** of the following: A. **Adalimumab Product: Adalimumab-adaz/Hyrimoz** (by Sandoz/Novartis)**, Adalimumab – adbm/Cyltezo**, **Adalimumab-ryvk/Simlandi** or **Humira** (by AbbVie) [requires prior authorization] B. **Enbrel** [requires prior authorization] C. **Otezla** [requires prior authorization] D. **Rinvoq** [requires prior authorization] E. **Skyrizi SC** [requires prior authorization] F. **Stelara SC** [requires prior authorization] G. **Taltz** [requires prior authorization] H. **Tremfya** [requires prior authorization] I. **Xeljanz/XR** [requires prior authorization] A.

Employer Group Plans	
Condition(s)	**Non-Preferred Product Criteria**
Rheumatoid Arthritis	Documentation of failure, contraindication, or intolerance to **TWO** of the following: A. **Actemra SC** [requires prior authorization] B. **Adalimumab Product: Adalimumab-adaz/Hyrimoz** (by Sandoz/Novartis)**, Adalimumab – adbm/Cyltezo**, **Adalimumab-ryvk/Simlandi,** or **Humira** (by AbbVie) [requires prior authorization] C. **Enbrel** [requires prior authorization] D. **Rinvoq** [requires prior authorization] E. **Xeljanz/XR** [requires prior authorization] A.

Individual and Family Plans	
Condition(s)	**Non-Preferred Product Criteria**
Polyarticular Juvenile Idiopathic Arthritis	Documentation of failure, contraindication, or intolerance to **TWO** of the following: A. **Actemra SC** [requires prior authorization] B. **Adalimumab Product: Adalimumab-adaz/Hyrimoz** (by Sandoz/Novartis)**, Adalimumab – adbm/Cyltezo**, **Adalimumab-ryvk/Simlandi,** or **Humira** (by AbbVie) [requires prior authorization] C. **Enbrel** [requires prior authorization] D. **Xeljanz/Xeljanz Oral Solution** [requires prior authorization
Psoriatic Arthritis - Adult	Documentation of failure, contraindication, or intolerance to **THREE** of the following: A. **Adalimumab Product: Adalimumab-adaz/Hyrimoz** (by Sandoz/Novartis)**, Adalimumab – adbm/Cyltezo**, **Adalimumab-ryvk/Simlandi,** or **Humira** (by AbbVie) [requires prior authorization] B. **Cimzia** [requires prior authorization] C. **Cosentyx** [requires prior authorization] D. **Enbrel** [requires prior authorization] E. **Otezla** [requires prior authorization] F. **Rinvoq** [requires prior authorization] G. **Skyrizi SC** [requires prior authorization] H. **Stelara SC** [requires prior authorization] I. **Tremfya** [requires prior authorization] J. **Xeljanz/XR** [requires prior authorization]
Rheumatoid Arthritis	Documentation of failure, contraindication, or intolerance to **TWO** of the following: A. **Actemra SC** [requires prior authorization] B. **Adalimumab Product: Adalimumab-adaz/Hyrimoz** (by Sandoz/Novartis)**, Adalimumab – adbm/Cyltezo**, **Adalimumab-ryvk/Simlandi,** or **Humira** (by AbbVie) [requires prior authorization] C. **Cimzia** [requires prior authorization] D. **Enbrel** [requires prior authorization] E. **Rinvoq** [requires prior authorization] F. **Xeljanz/XR** [requires prior authorization]

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of abatacept (Orencia) subcutaneous is considered medically necessary for **ALL** covered diagnoses when initial criteria are met AND beneficial response is demonstrated.

Authorization Duration

Initial approval duration is up to 12 months.
Reauthorization approval duration is up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven, including the following (this list may not be all inclusive):

1. **Ankylosing Spondylitis.** In an open-label Phase II trial, Orencia was administered intravenously on Days 1, 15, 29, and every 28 days thereafter to patients with active ankylosing spondylitis.[5] Patients received a fixed dosage of Orencia of approximately 10 mg/kg based on body weight. The primary endpoint was a 40% improvement in disease activity at Week 24 in the Assessment of SpondyloArthritis international Society criteria (ASAS 40). At Week 24, the ASAS 40 was 13.3% (n = 2/15) in tumor necrosis factor inhibitor (TNFi)-naïve patients compared with no responses in patients who had previously failed TNFis (n = 15). ASAS 20 response was 26.7% (n = 4/15) in TNFi-naïve patients compared with 20% (n = 3/15) in those who had previously failed TNFis. A major response was not shown with treatment to Orencia.

2. **Concurrent Use with a Biologic or with a Targeted Synthetic DMARD.** Orencia subcutaneous should not be administered in combination with another biologic or with a targeted synthetic DMARD used for an inflammatory condition (see Appendix for examples).[1] Combination therapy is generally not recommended due to a higher rate of adverse events with combinations and lack of data supportive of additional efficacy.

   This does NOT exclude the use of conventional synthetic DMARDs (e.g., methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with Orencia subcutaneous.

3. **Inflammatory Bowel Disease (i.e., Crohn's Disease, Ulcerative Colitis).** In placebo-controlled trials evaluating the efficacy of Orencia intravenous for induction and maintenance in adults with active, moderate to severe Crohn's disease (n = 451) and ulcerative colitis (n = 490), Orencia was no more effective than placebo.[6] Patients were randomized to Orencia 30, 10, or 3 mg/kg (according to body weight) or placebo and dosed at Weeks 0, 2, 4, and 8. A total of 90 patients with Crohn's disease and 131 patients with ulcerative colitis who responded to induction were then randomized to Orencia 10 mg/kg or placebo every 4 weeks through Week 52. When used for induction of Crohn's disease, 17.2%, 10.2%, and 15.5% of patients receiving Orencia 30 mg, 10 mg, and 3 mg/kg achieved a clinical response at Weeks 8 and 12 compared with 14.4% of patients receiving placebo (P = not significant [NS] for all comparisons). In patients with Crohn's disease, response and remission at Week 52 was not significantly different between the Orencia intravenous and placebo treatment groups. When used as induction therapy in ulcerative colitis, 21.4%, 19.0%, and 20.3% of patients receiving Orencia 30 mg, 10 mg, and 3 mg/kg achieved a clinical response at Week 12 compared with 29.5% of patients receiving placebo (P = 0.043 for 10 mg/kg vs. placebo; other comparisons P = NS). At Week 52, 12.5% (n = 8/64) and 14.1% (n = 9/64) of patients with ulcerative colitis were in remission (P = NS) and 17.2% of patients in each treatment group (n = 11/64 for each group) had achieved a response.

4. **Psoriasis**. In the pivotal trial evaluating Orencia subcutaneous for psoriatic arthritis, there was not a significant difference at Week 24 in the proportion of patients with a 50% reduction in the Psoriasis Area and Severity Index (PASI 50) response vs. placebo ± conventional synthetic (cs)DMARD (27% vs. 20% with placebo ± csDMARD; P = NS).[8] In a multicenter, Phase I, 26-week, open-label dose-escalation study, 43 patients with stable plaque psoriasis (10% to 49% body surface area involvement) received four doses of Orencia given as a 1-hour intravenous infusion on Days 1, 3, 16 and 29.[7] The starting dose was 0.5 mg/kg. Four to six patients were accrued to each of eight dose levels: 0.5, 1, 2, 4, 8, 16, 25 and 50 mg/kg. A

parallel control group was matched for age and overall disease severity. In all, 46% of patients on Orencia achieved a 50% or greater sustained improvement in clinical disease activity (Physician's Global Assessment of disease activity) compared with baseline psoriasis evaluation. Progressively greater effects were observed with the highest doses. Further studies are needed to establish safety and efficacy, as well as appropriate dosing, in plaque psoriasis.

Background

OVERVIEW

Orencia subcutaneous, a selective T-cell costimulation modulator, is indicated for the following uses:[1]

- **Rheumatoid arthritis**, in adults with moderately to severely active disease.
- **Juvenile idiopathic arthritis**, in patients ≥ 2 years of age with moderately to severely active polyarticular disease.
- **Psoriatic arthritis**, in adults with active disease.

Orencia is not recommended for use concomitantly with other potent immunosuppressants such as biologics or Janus kinase inhibitors.

Guidelines

Orencia is addressed in guidelines for treatment of various inflammatory conditions.

- **Rheumatoid Arthritis:** Guidelines from the American College of Rheumatology (ACR) [2021] recommend addition of a biologic or a targeted synthetic disease-modifying antirheumatic drug (DMARD) for a patient taking the maximum tolerated dose of methotrexate who is not at target.[2]
- **Juvenile Idiopathic Arthritis:** Guidelines from ACR (2019) list biologics among the treatment options for subsequent therapy in patients with polyarthritis.[3] Initial therapy with a biologic may be considered for patients with risk factors and involvement of high-risk joints (e.g., cervical spine, wrist, or hip), high disease activity, and/or those judged to be at high risk of disabling joint damage. In patients with active sacroiliitis or enthesitis despite nonsteroidal anti-inflammatory drug, a tumor necrosis factor inhibitor (TNFi) is recommended.
- **Psoriatic Arthritis:** Guidelines from ACR (2018) recommend TNFis over other biologics for use in treatment-naïve patients with psoriatic arthritis and in those who were previously treated with an oral therapy.[4] However, Orencia may be considered over other biologics in patients with recurrent or serious infections.

References

1. Orencia® for injection [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; June 2021.
2. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol*. 2021;73(7):1108-1123.
3. Ringold S, Angeles-Han ST, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for non-systemic polyarthritis, sacroiliitis, and enthesitis. *Arthritis Rheumatol*. 2019;71(6):717-734.
4. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis. *Arthritis Care Res (Hoboken)*. 2019;71(1):2-29.
5. Song IH, Heldmann F, Rudwaleit M, et al. Treatment of active ankylosing spondylitis with abatacept: an open-label, 24-week pilot study. *Ann Rheum Dis*. 2011;70(6):1108-1110.
6. Sandborn WJ, Colombel JF, Sands BE, et al. Abatacept for Crohn's disease and ulcerative colitis. *Gastroenterology*. 2012;143(1):62-69.e4.
7. Abrams JR, Lebwohl MG, Guzzo CA, et al. CTLA4Ig-mediated blockade of T-cell costimulation in patients with psoriasis vulgaris. *J Clin Invest*. 1999;103:1243-1252.
8. Mease PJ, Gottlieb AB, van der Heijde D, et al. Efficacy and safety of abatacept, a T-cell modulator, in a randomised, double-blind, placebo-controlled, phase III study in psoriatic arthritis. *Ann Rheum Dis*. 2017;76(9):1550-1558.

APPENDIX

Table 1. Approved TNFis for Targeted Indications.

	Rheumatology					Dermatology	Gastroenterology	
	RA	JIA	AS	nr-axSpA	PsA	PsO	CD	UC
Tumor Necrosis Factor Inhibitors								
Cimzia	√	--	√	√	√	√	√	--
Enbrel	√	√	√	--	√	√	--	--
Adalimumab products (Humira, biosimilars)	√	√	√	--	√	√	√	√
Infliximab Products	√	--	√	--	√	√	√	√
Simponi Subcutaneous	√	--	√	--	√	--	--	√
Simponi Aria	√	√	√	--	√	--	--	--

TNFis – Tumor necrosis factor inhibitors; RA – Rheumatoid arthritis; JIA – Juvenile idiopathic arthritis; AS – Ankylosing spondylitis; nr-axSpA – Non-radiographic spondyloarthritis; PsA – Psoriatic arthritis; PsO – Plaque psoriasis; CD – Crohn's disease; UC – Ulcerative colitis.

Table 2. Approved IL-17, IL-23, and IL-12/23 Blockers for Targeted Indications.

	Rheumatology			Dermatology	Gastroenterology	
	Ankylosing Spondylitis	nr-axSpA	Psoriatic Arthritis	Plaque Psoriasis	Crohn's Disease	Ulcerative Colitis
Interleukin-17 Blockers						
Cosentyx	√	√	√	√	--	--
Siliq	--	--	--	√	--	--
Taltz	√	√	√	√	--	--
Interleukin-23 Blockers						
Ilumya	--	--	--	√	√	--
Skyrizi Intravenous	--	--	--	--	√#	--
Skyrizi Subcutaneous	--	--	√	√	√^	--
Tremfya	--	--	√	√	--	--
Interleukin-12/23 Blockers						
Stelara Subcutaneous	--	--	√	√	√^	√^
Stelara Intravenous	--	--	--	--	√#	√#

IL – Interleukin; nr-axSpA – Non-radiographic spondyloarthritis; ^ Maintenance dosing only; # Induction dosing only

Table 3. Approved Oral tsDMARDs for Targeted Indications.

	Rheumatology					Dermatology	Gastro-enterology
	Rheumatoid Arthritis	Juvenile Idiopathic Arthritis	Ankylosing Spondylitis	nr-axSpA	Psoriatic Arthritis	Plaque Psoriasis	Ulcerative Colitis
Janus Kinases Inhibitors							
Olumiant	√	--	--	--	--	--	--
Rinvoq	√	--	√	√	√	--	√
Xeljanz tablets	√	√#	√	--	√	--	√
Xeljanz oral solution	--	√#	--	--	--	--	--
Xeljanz XR	√	--	√	--	√	--	√
Phosphodiesterase Type 4 Inhibitor							
Otezla	--	--	--	--	√	√	--
Sphingosine 1-Phosphate Receptor Modulator							
Zeposia	--	--	--	--	--	--	√

	Rheumatology					Dermatology	Gastro-enterology
	Rheumatoid Arthritis	Juvenile Idiopathic Arthritis	Ankylosing Spondylitis	nr-axSpA	Psoriatic Arthritis	Plaque Psoriasis	Ulcerative Colitis
Tyrosine Kinase 2 Inhibitor							
Sotyktu	--	--	--	--	--	√	--

tsDMARDs – Targeted synthetic disease-modifying antirheumatic drugs; # Indicated in polyarticular JIA.

Table 4. Other Approved Biologics for Targeted Indications.

	Rheumatology		
	Rheumatoid Arthritis	Juvenile Idiopathic Arthritis	Psoriatic Arthritis
Interleukin-6 Blockers			
Actemra Intravenous	√	√^	--
Actemra Subcutaneous	√	√^	--
Kevzara	√	--	--
Interleukin-1 Blocker			
Kineret	√	--	--
T-Cell Costimulation Modulator			
Orencia Intravenous	√	√#	√
Orencia Subcutaneous	√	√#	√
CD20-Directed Cytolytic Antibody			
Rituximab Intravenous Products	√	--	--

^ Indicated in polyarticular and systemic JIA; # Indicated in polyarticular JIA.