

POLICY: Inflammatory Conditions – Orencia® (abatacept for intravenous infusion)

EFFECTIVE DATE: 1/1/2020

LAST REVISION DATE: 09/16/2024

COVERAGE CRITERIA FOR: All UCare Plans

OVERVIEW

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

1. **Graft-versus-host disease (GVHD)**, for prophylaxis of acute GVHD in combination with a calcineurin inhibitor and methotrexate, in patients ≥ 2 years of age undergoing hematopoietic stem cell transplantation from a matched or 1 allele-mismatched unrelated donor.
2. **Juvenile idiopathic arthritis**, in patients ≥ 2 years of age with moderately to severely active polyarticular disease.
3. **Psoriatic arthritis (PsA)**, in adults with active disease.
4. **Rheumatoid arthritis**, in adults with moderately to severely active disease.

Orencia is not recommended for use concomitantly with other potent immunosuppressants such as biologics or Janus kinase inhibitors. Orencia is available as an intravenous infusion that is dosed on body weight. There is also a subcutaneous injection available in prefilled syringes. Some patients initiating therapy with Orencia subcutaneous will receive a single loading dose with Orencia intravenous.

Guidelines

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

- **GVHD:** Guidelines for hematopoietic cell transplantation for pre-transplant recipient evaluation and management of GVHD are available from the National Comprehensive Cancer Network (NCCN) [version 3.2023 – October 9, 2023].⁹ Immunosuppressive agents are commonly used for the prevention of GVHD. Orencia is among the therapies listed for treatment of steroid-refractory chronic GVHD.
- **Juvenile Idiopathic Arthritis:** Guidelines from American College of Rheumatology (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 use, a tumor necrosis factor inhibitor (TNFi) is recommended.

- **PsA:** Guidelines from ACR (2018) recommend TNFis over other biologics for use in treatment-naïve patients with PsA 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.
- **Rheumatoid Arthritis:** Guidelines from the ACR (2021) recommend addition of a biologic or a targeted synthetic disease modifying anti-rheumatic drug (DMARD) for a patient taking the maximum tolerated dose of methotrexate who is not at target.²

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Orencia intravenous. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). Because of the specialized skills required for evaluation and diagnosis of patients treated with Orencia intravenous as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Orencia intravenous to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. For prevention of GVHD, the approval duration is for 30 days, which is an adequate duration for the patient to receive four doses.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Orencia intravenous is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Graft-Versus-Host Disease – Prevention.** Approve for 4 doses if the patient meets ALL of the following (A, B, C, D, E, and F):
 - A) Patient is ≥ 2 years of age; AND
 - B) Orencia is being used for prevention of acute graft-versus-host disease; AND
 - C) Patient will also receive a calcineurin inhibitor for prevention of acute graft-versus-host disease; AND
Note: Examples of calcineurin inhibitors include cyclosporine and tacrolimus.
 - D) Patient will also receive methotrexate for prevention of acute graft-versus-host disease; AND
 - E) Patient will undergo hematopoietic stem cell transplantation from one of the following donors (i or ii):

- i. Matched unrelated donor; OR
 - ii. 1-allele-mismatched unrelated donor; AND
- F) The medication is prescribed by or in consultation with an oncologist, hematologist, or a physician affiliated with a transplant center.

Dosing. Approve if dosing meets the following (A and B):

- A) The dose meets ONE of the following (i or ii):
- i. Patient is ≥ 6 years of age: Approve up to 10 mg/kg to a maximum of 1,000 mg per dose; OR
 - ii. Patient is ≥ 2 and < 6 years of age: Approve up to 15 mg/kg.
- B) A dose is administered the day before transplantation, then on Days 5, 14, and 28 after transplantation.

2. Juvenile Idiopathic Arthritis (JIA). Approve for the duration noted if the patient meets ONE of the following (A or B):

Note: This includes JIA regardless of type of onset. JIA is also referred to as Juvenile Rheumatoid Arthritis.

- A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and ii):
- i. Patient is ≥ 2 years of age; AND
 - ii. Patient meets ONE of the following (a, b, c, or d):
 - a) Patient has tried one other agent for this condition; OR

Note: Examples of therapies which could have been tried include methotrexate, sulfasalazine, leflunomide, and a nonsteroidal anti-inflammatory drug (NSAID). A biologic other than the requested drug also counts as a trial of one agent for JIA. A biosimilar of the requested biologic does not count. Refer to [Appendix](#) for examples of biologics used for JIA.
 - b) Patient will be starting on therapy concurrently with methotrexate, sulfasalazine, or leflunomide; OR
 - c) Patient has an absolute contraindication to methotrexate, sulfasalazine, or leflunomide; OR

Note: Examples of absolute contraindications to methotrexate include pregnancy, breast feeding, alcoholic liver disease, immunodeficiency syndrome, blood dyscrasias.
 - d) Patient has aggressive disease, as determined by the prescriber; AND
 - iii. The medication is prescribed by or in consultation with a rheumatologist.
- B) Patient is Currently Receiving Ocrencia (Intravenous or Subcutaneous). Approve for 1 year if the patient meets BOTH of the following (i and ii):
- i. Patient has been established on therapy for at least 6 months; AND

Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).
 - ii. Patient meets at least ONE of the following (a or b):

- a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of objective measures include Physician Global Assessment (MD global), Parent/Patient Global Assessment of Overall Well-Being (PGA), Parent/Patient Global Assessment of Disease Activity (PDA), Juvenile Arthritis Disease Activity Score (JDAS), Clinical Juvenile Arthritis Disease Activity Score (cJDAS), Juvenile Spondyloarthritis Disease Activity Index (JSpADA), serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), and/or reduced dosage of corticosteroids.
- b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as improvement in limitation of motion, less joint pain or tenderness, decreased duration of morning stiffness or fatigue, improved function or activities of daily living.

Dosing. Approve if dosing meets the following (A and B):

- A) The weight-based dose meets ONE of the following (i, ii, or iii):
 - i. 10 mg/kg if the patient weighs < 75 kg; OR
 - ii. 750 mg if the patient weighs 75 kg to 100 kg; OR
 - iii. 1,000 mg if the patient weighs > 100 kg; AND
- B) The dose is administered at Weeks 0, 2, and 4, then every 4 weeks thereafter.

3. **Psoriatic Arthritis.** Approve for the duration noted if the patient meets ONE of the following (A or B):

- A) Initial Therapy. Approve for 6 months if the patient meets BOTH of the following (i and ii):
 - i. Patient is \geq 18 years of age; AND
 - ii. The medication is prescribed by or in consultation with a rheumatologist or a dermatologist.
- B) Patient is Currently Receiving Orencia (Intravenous or Subcutaneous). Approve for 1 year if the patient meets BOTH of the following (i and ii):
 - i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).
 - ii. Patient meets at least ONE of the following (a or b):
 - a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requesting drug); OR
Note: Examples of standardized measures of disease activity include Disease Activity Index for Psoriatic Arthritis (DAPSA), Composite Psoriatic Disease Activity Index (CPDAI), Psoriatic Arthritis Disease Activity Score (PsA DAS), Grace Index, Leeds Enthesitis Score (LEI), Spondyloarthritis Consortium of Canada (SPARCC) enthesitis score, Leeds Dactylitis Instrument Score, Minimal Disease Activity (MDA), Psoriatic Arthritis Impact of Disease (PsAID-12), and/or serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).

- b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths.

Dosing. Approve if dosing meets the following (A and B):

- A) The dose is based on the patient's weight and meets ONE of the following (i, ii, or iii):
- i. 500 mg if the patients weighs < 60 kg; OR
 - ii. 750 mg if the patient weighs 60 kg to 100 kg; OR
 - iii. 1,000 mg if the patient weighs > 100 kg; AND
- B) The dose is administered at Weeks 0, 2, and 4, then every 4 weeks thereafter.

4. **Rheumatoid Arthritis.** Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):

- i. Patient is \geq 18 years of age; AND
- ii. Patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months; AND

Note: Examples of conventional synthetic DMARDs include methotrexate (oral or injectable), leflunomide, hydroxychloroquine, and sulfasalazine. An exception to the requirement for a trial of one conventional synthetic DMARD can be made if the patient has already had a 3-month trial of at least one biologic other than the requested drug. A biosimilar of the requested biologic does not count. Refer to [Appendix](#) for examples of biologics used for rheumatoid arthritis. A patient who has already tried a biologic is not required to “step back” and try a conventional synthetic DMARD.

iii. The medication is prescribed by or in consultation with a rheumatologist.

B) Patient is Currently Receiving Orencia (Intravenous or Subcutaneous). Approve for 1 year if the patient meets BOTH of the following (i and ii):

- i. Patient has been established on therapy for at least 6 months; AND

Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least ONE of the following (a or b):

- a) Patient experienced a beneficial clinical response when assessed by at least one objective measure; OR

Note: Examples of standardized and validated measures of disease activity include Clinical Disease Activity Index (CDAI), Disease Activity Score (DAS) 28 using erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), Patient Activity Scale (PAS)-II, Rapid Assessment of Patient Index Data 3 (RAPID-3), and/or Simplified Disease Activity Index (SDAI).

- b) Patient experienced an improvement in at least one symptom, such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths.

Dosing. Approve if dosing meets the following (A and B):

- A) The dose is based on the patient's weight and meets ONE of the following (i, ii, or iii):
- i. 500 mg if the patients weighs < 60 kg; OR
 - ii. 750 mg if the patient weighs 60 kg to 100 kg; OR
 - iii. 1,000 mg if the patient weighs > 100 kg; AND
- B) The dose is administered at Weeks 0, 2, and 4, then every 4 weeks thereafter.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Orencia intravenous is not recommended in the following situations:

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 Oral Small Molecule Drug.** This medication should not be administered in combination with another biologic or with a targeted synthetic oral small molecule drug used for an inflammatory condition (see [Appendix](#) for examples). Combination therapy is generally not recommended due to a potentially higher rate of adverse events and lack of controlled clinical data supporting additive efficacy.
Note: This does NOT exclude the use of conventional synthetic DMARDs (e.g., methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine) in combination with this medication.
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.** (Note: Patients with concomitant plaque psoriasis and psoriatic arthritis may be reviewed under the psoriatic arthritis criteria above.) 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.
5. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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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.

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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.
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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	02/22/2023
Annual Revision	No criteria changes.	03/13/2024
Selected Revision	Juvenile Idiopathic Arthritis: For initial approvals, a requirement that the patient is ≥ 2 years of age was added. Psoriatic Arthritis: For initial approvals, a requirement that the patient is ≥ 18 years of age was added. Rheumatoid Arthritis: For initial approvals, a requirement that the patient is ≥ 18 years of age was added. Conditions Not Recommended for Approval: Concurrent use with a Biologic or with a Targeted Synthetic Oral Small Molecule Drug was changed to as listed (previously oral small molecule drug was listed as Disease-Modifying Antirheumatic Drug).	09/11/2024
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024

APPENDIX

	Mechanism of Action	Examples of Inflammatory Indications*
Biologics		
Adalimumab SC Products (Humira [®] , biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
Cimzia[®] (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel [®] , biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA
Zymfentra[®] (infliximab-dyyb SC injection)	Inhibition of TNF	CD, UC
Infliximab IV Products (Remicade [®] , biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Simponi[®], Simponi[®] Aria[™] (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC IV formulation: AS, PJIA, PsA, RA
Actemra[®] (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA IV formulation: PJIA, RA, SJIA
Kezara[®] (sarilumab SC injection)	Inhibition of IL-6	RA, PMR
Orencia[®] (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PSA, RA IV formulation: JIA, PsA, RA
Rituximab IV Products (Rituxan [®] , biosimilars)	CD20-directed cytolytic antibody	RA
Kineret[®] (anakinra SC injection)	Inhibition of IL-1	JIA [^] , RA
Stelara[®] (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC IV formulation: CD, UC
Siliq[™] (brodalumab SC injection)	Inhibition of IL-17RA	PsO
Bimzelx[®] (bimekizumab-bkzx SC injection)	Inhibition of IL-17A and IL-17F	PsO
Cosentyx[®] (secukinumab SC injection, secukinumab IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, nr-axSpA, PsO, PsA IV formulation: AS, nr-axSpA, PsA
Taltz[®] (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Ilumya[™] (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Omvoh[®] (mirikizumab-mrkz SC injection, mirikizumab-mrkz IV infusion)	Inhibition of IL-23	UC
Skyrizi[®] (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PSA, PsO IV formulation: CD
Tremfya[™] (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio[™] (vedolizumab IV infusion, vedolizumab SC injection)	Integrin receptor antagonist	SC formulation: UC IV formulation: CD, UC
Oral Therapies/Targeted Synthetic DMARDs		
Otezla[®] (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo[™] (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant[®] (baricitinib tablets)	Inhibition of JAK pathways	RA
Rinvoq[®] (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, AS, nr-axSpA, RA, PsA, UC
Sotyktu[™] (deucravacitinib tablets)	Inhibition of TYK2	PsO
Xeljanz[®] (tofacitinib tablets)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
Xeljanz[®] XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC
Velsipity[®] (etrasimod tablets)	Sphingosine 1 phosphate receptor modulator	UC
Zeposia[®] (ozanimod tablets)	Sphingosine 1 phosphate receptor modulator	UC

* Not an all-inclusive list of indications (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn’s disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; IV – Intravenous, PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic arthritis; PMR – Polymyalgia rheumatic; ^ Off-label use of Kineret in JIA supported in guidelines; ERA – Entesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis; TYK2 – Tyrosine kinase 2.