abatacept (Orencia®) intravenous

Medicare Advantage Medical Policy #MA-140
Original Effective Date: 01/01/2026
Current Effective Date: 01/01/2026

Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Per the Self-Administered Drug list as defined by the Medicare Administrative Contractor for the Health Plan, subcutaneous abatacept (Orencia®)‡ is eligible for coverage under Part D only and not targeted by this policy.

Rheumatoid Arthritis

Based on review of available data, the Health Plan may consider intravenous abatacept (Orencia®)‡ for the treatment of rheumatoid arthritis to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for the use of intravenous abatacept (Orencia) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; AND
- Patient has moderately to severely active rheumatoid arthritis; AND
- Patient has failed treatment with one or more traditional disease-modifying anti-rheumatic drugs (DMARDs), such as methotrexate, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
- Orencia may be used alone or in combination with traditional DMARDs; AND
- Orencia is NOT given concomitantly with biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), or other drugs such as apremilast (Otezla®)‡ or tofacitinib (Xeljanz/XR); AND
- Patient has a negative tuberculosis (TB) test (e.g., purified protein derivative [PPD], blood test) prior to treatment.

Polyarticular Juvenile Idiopathic Arthritis

Based on review of available data, the Health Plan may consider the use of intravenous abatacept (Orencia) for the treatment of moderately to severely active polyarticular juvenile idiopathic arthritis to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for the use of intravenous abatacept (Orencia) will be considered when all of the following criteria met:

- Patient is 6 years of age or older; AND
- Patient has moderately to severely active polyarticular juvenile idiopathic arthritis; AND
- Patient has failed treatment with one or more traditional DMARDs, such as methotrexate, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
- Orencia may be used as monotherapy or concomitantly with methotrexate; AND
- Orencia is NOT given concomitantly with biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), or other drugs such as apremilast (Otezla) or tofacitinib (Xeljanz/XR); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Psoriatic Arthritis

Based on review of available data, the Health Plan may consider intravenous abatacept (Orencia) for the treatment of psoriatic arthritis to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for the use of intravenous abatacept (Orencia) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; AND
- Patient has psoriatic arthritis; AND
- Patient has failed treatment with one or more traditional DMARDs, such as methotrexate, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
- Orencia is NOT given concomitantly with biologic DMARDs, such as adalimumab (Humira, biosimilars) or etanercept (Enbrel), or other drugs such as apremilast (Otezla) or tofacitinib (Xeljanz/XR); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Prophylaxis of Acute Graft Versus Host Disease

Based on review of available data, the Health Plan may consider the use of intravenous abatacept (Orencia) for the prophylaxis of acute graft versus host disease to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for the use of intravenous abatacept (Orencia) will be considered when all of the following criteria met:

- Patient is 2 years of age or older; AND
- Patient is undergoing hematopoietic stem cell transplantation from a matched or 1 allele-mismatched unrelated donor; AND
- Patient will be using the requested drug in combination with a calcineurin inhibitor (i.e. cyclosporine or tacrolimus) and methotrexate; AND
- Dosing is as follows:

  - For patients 6 years of age and older: 10 mg/kg (maximum dose 1,000 mg) on the day before transplantation, followed by doses on days 5, 14, and 28 after transplant; OR
  - For patients 2 years to less than 6 years of age: 15 mg/kg on the day before transplantation, followed by a 12 mg/kg dose on days 5, 14, and 28 after transplant.
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

When Services Are Considered Not Medically Necessary

Based on review on available data, the Health Plan considers the use of intravenous abatacept (Orencia) when any of the following criteria for their respective disease state listed below (and denoted in the patient selection criteria above) are not met to be **not medically necessary**:**

- For adult rheumatoid arthritis:
  - Patient has failed treatment with one or more traditional DMARDs
- For polyarticular juvenile idiopathic arthritis:
  - Patient has failed treatment with one or more traditional DMARDS
- For adult psoriatic arthritis:
  - Patient has failed treatment with one or more traditional DMARDs

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of intravenous abatacept (Orencia) when patient selection criteria are not met to be **investigational*** (with the exception of those denoted above as not **medically necessary****).

Based on review of available data, the Health Plan considers the use of intravenous abatacept (Orencia) for indications other than those listed above to be **investigational.***

Background/Overview

Orencia is an injectable synthetic protein produced by recombinant deoxyribonucleic acid (DNA) technology that is used for the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, and for the prophylaxis of acute graft versus host disease. Orencia is a selective costimulation modulator that binds to CD80 and CD86 to block the interaction with CD28 required for full T lymphocyte (T cell) activation. Activated T cells have been found in the synovium of patients with rheumatoid arthritis. These activated T cells multiply and release chemicals that cause destruction of tissues around the joints, and cause symptoms of rheumatoid arthritis.

Orencia comes as a lyophilized power for intravenous infusion that provides 250 mg of Orencia in a 15 mL vial. Orencia also comes in a 125 mg/mL single dose prefilled ClickJect autoinjector for subcutaneous use in patients with rheumatoid arthritis and psoriatic arthritis. More recently, 50 mg/0.4mL and 87.5 mg/0.7 mL strengths are available in a single dose prefilled syringe for subcutaneous use in juvenile idiopathic arthritis. There is also a 125 mg single dose prefilled syringe that can be used subcutaneously in any of the indications. Only the lyophilized powder for intravenous use is approved for use in the prophylaxis of acute graft versus host disease, in which dosing varies by age. See the package insert for complete details.

Rheumatoid Arthritis
Rheumatoid Arthritis is a chronic (long-term) disease that causes inflammation of the joints and surrounding tissues. It can also affect other organs. It is considered an autoimmune disease. In an autoimmune disease, the immune system confuses healthy tissue for foreign substances. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Juvenile Idiopathic Arthritis
Polyarticular juvenile idiopathic arthritis and systemic juvenile idiopathic arthritis are types of juvenile idiopathic arthritis, a chronic form of arthritis in children. Polyarticular juvenile idiopathic is characterized by inflammation in five or more joints within the first six months of the disease, while in systemic juvenile idiopathic arthritis, many of the signs and symptoms (such as rash and fever) affect the whole body, and not just the joints. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Psoriatic Arthritis
Psoriatic arthritis is an arthritis that is often associated with psoriasis of the skin. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Traditional Disease-Modifying Anti-Rheumatic Drugs
Traditional disease-modifying anti-rheumatic drugs are typically used for the treatment of inflammatory conditions. These drugs slow the disease process by modifying the immune system.

- methotrexate
- cyclosporine
- sulfasalazine
- mercaptopurine
- gold compounds

Graft Versus Host Disease
Graft versus host disease is a common occurrence in hematopoietic stem cell transplants. It occurs when immune cells from a non-identical donor recognize the host (transplant recipient) as foreign.

This causes an immune reaction, which can cause significant morbidity and mortality. Typical organs targeted are the skin, gastrointestinal tract, and liver. It is common for a calcineurin inhibitor (such as cyclosporine or tacrolimus) plus methotrexate to be used to prevent acute graft versus host disease.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Orencia is approved for the treatment of moderately to severely active rheumatoid arthritis in adults. Orencia is also approved to treat juvenile idiopathic arthritis in patients 2 years of age and older. It should be noted that the intravenous form of Orencia for use in juvenile idiopathic arthritis is only approved for those 6 years of age or older. In 2017, Orencia also gained an indication for use in adults with psoriatic arthritis. In late 2021, Orencia was approved for the prophylaxis of acute graft versus host disease, in combination with a calcineurin inhibitor and methotrexate, in adults and pediatric patients 2 years of age and older undergoing hematopoietic stem cell transplantation from a matched or 1 allele-mismatched unrelated donor.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Rheumatoid Arthritis

The approval of Orencia for adult rheumatoid arthritis is based on outcome data from three double blind, randomized, placebo-controlled trials that evaluated the biologic agent in adults with rheumatoid arthritis who had an unsuccessful response to other rheumatoid arthritis drugs. These trials include the Abatacept Trial in Treatment of Anti-TNF Inadequate responders (ATTAIN), Abatacept in Inadequate responders to Methotrexate (AIM), and Abatacept Study of Safety in Use with other RA therapies (ASSURE).

In the AIM study, which was a one year placebo controlled Phase III trial using a fixed dose of Orencia in patients with active rheumatoid arthritis despite methotrexate treatment. This study showed that Orencia plus methotrexate inhibits radiographic progression of joint damage significantly better than placebo plus methotrexate.

The purpose of the ASSURE trial was to assess the safety of combination therapy with Orencia and approved biologic and non-biologic DMARDs in patients with active rheumatoid arthritis. This study showed that Orencia and placebo have a similar safety profile when added to DMARD therapy in patients with active rheumatoid arthritis and co-morbidities. However, Orencia added with

biologic therapy showed the least favorable profile with increased incidences of adverse events and infections.

The ATTAIN study is a randomized, double blind, phase III trial that evaluated the efficacy of Orencia in patients with active rheumatoid arthritis and an inadequate response to anti-TNF-alpha therapy. In both phase III studies (AIM and ATTAIN), Orencia demonstrated significant improvement in the signs and symptoms of rheumatoid arthritis as measured by the American College of Rheumatology (ACR) scoring system. Significant improvements in physical function were noted as compared to placebo. These improvements were maintained up to three years in a Phase II trial of patients with inadequate response to methotrexate.

Polyarticular Juvenile Idiopathic Arthritis
The approval of intravenous Orencia for juvenile idiopathic arthritis was assessed in a three part study (JIA-1) in patients 6-17 years of age. The ACR scores were assessed in these patients at the end of the first part of the study and the pediatric ACR 30/50/70 responses were 65%, 50%, and 28%, respectively. Period B included a withdrawal phase and patients on Orencia had fewer disease flares than those patients treated with placebo. The last part of the trial was an open label extension. The approval of subcutaneous Orencia for juvenile idiopathic arthritis without an intravenous loading dose was assessed in study JIA-2, which was a 2 period, open label study that included children 2 to 17 years of age. At study entry, 80% of subjects were taking methotrexate and remained stable on their dose of methotrexate. The ACR 30/50/70 responses assessed at 4 months in the 2 to 17 year old patients were consistent with the results from the intravenous study, JIA-1.

Psoriatic Arthritis
Orencia was assessed in 594 patients with psoriatic arthritis in two trials. The primary endpoint for both trials was the proportion of patients achieving an ACR20 response at week 24. A higher proportion of patients achieved an ACR20 response after treatment with Orencia as compared to placebo at week 24.

Prophylaxis of Acute Graft Versus Host Disease
The efficacy of Orencia, in combination with a calcineurin inhibitor and methotrexate, for the prophylaxis of acute graft versus host disease (aGVHD), was evaluated in a multicenter, two cohort clinical study (GVHD-1) in patients age 6 years and older who underwent hematopoietic stem cell transplantation (HSCT) from a matched or 1 allele-mismatched unrelated donor (URD). The two cohorts in GVHD-1 included: 1) an open-label, single-arm study of 43 patients who underwent a 7 of 8 Human Leukocyte Antigen (HLA)-matched HSCT (7 of 8 cohort); and 2) a randomized (1:1), double-blind, placebo-controlled study of patients who underwent an 8 of 8 HLA-matched HSCT who received Orencia or placebo in combination with a calcineurin inhibitor and methotrexate (8 of 8 cohort). In both the 7/8 and 8/8 cohorts, Orencia was administered at a dose of 10 mg/kg (1,000 mg maximum dose) as an intravenous infusion over 60 minutes, beginning on the day before transplantation (Day -1), followed by administration on Days 5, 14, and 28 after transplantation.

Efficacy was established based on overall survival (OS) and grade II-IV aGVHD free survival (GFS) results assessed at Day 180 post-transplantation. Overall survival was 97% in the Orencia plus a calcineurin inhibitor and methotrexate group vs. 84% in the calcineurin inhibitor and methotrexate alone group [HR 0.33 (0.12, 0.93)]. Orencia plus a calcineurin inhibitor and methotrexate did not significantly improve grade III-IV GFS versus placebo plus a calcineurin inhibitor and methotrexate at Day 180 post-transplantation [87% vs. 75%, HR 0.55 (0.26, 1.18)].

In an exploratory analysis of the 7 of 8 cohort of Orencia-treated patients (n=43), the rates of Grade III-IV GVHD-free survival, Grade II-IV GVHD-free survival, and overall survival at day 180 post-transplantation were 95% (95% CI 83%, 99%), 53% (95% CI 38%, 67%), and 98% (95% CI 85%, 100%), respectively.

Study GVHD-2 was a clinical study that used data from the Center for International Blood and Marrow Transplant Research (CIBMTR). The study analyzed outcomes of Orencia in combination with a calcineurin inhibitor and methotrexate, versus a calcineurin inhibitor and methotrexate alone, for the prophylaxis of aGVHD, in patients 6 years of age or older who underwent HSCT from a 1 allele-mismatched URD between 2011 and 2018. The Orencia plus calcineurin inhibitor and methotrexate treated group (n=54) included 42 patients from GVHD-1, in addition to 12 patients treated with Orencia outside of GVHD-1. The comparator group (n=162) was randomly selected in a 3:1 ratio to the Orencia-treated group from the CIBMTR registry from patients who had not received Orencia during the study period. Analyses used propensity score matching and inverse probability of treatment weighting to help address the impact of selection bias. Efficacy was based on Overall Survival (OS) at Day 180 post-HSCT. The OS rate at Day 180 in the Orencia in combination with calcineurin inhibitor and methotrexate group was 98% (95% CI: 78, 100) and the OS rate at Day 180 in the calcineurin inhibitor and methotrexate group was 75% (95% CI: 67, 82).

References

1. Orencia [package insert]. Bristol Myers Squibb. Princeton, New Jersey. Updated May 2024.
2. National Institute of Arthritis and Musculoskeletal and Skin Diseases. Juvenile Arthritis.https://www.niams.nih.gov/Health_Info/Juv_Arthritis/default.asp#7
3. Prevention of acute graft versus host disease. UpToDate.

Policy History

Original Effective Date: 01/01/2026
Current Effective Date: 01/01/2026
09/16/2025 UM Committee review and approval. New policy.
Next Scheduled Review Date: 09/2026

Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 by the American Medical

Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J0129
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or

3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the Health Plan Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.