| WellMed<br>Doctors helping patients for more than 25 years | **Effective Date: 12/21/22** | **Revision Date(s):**<br>01/22/18, 12/14/18, 01/21/20, 04/08/21, 8/19/22 |
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**Policy Number: 015.005**

**Title: Coverage Determination Policy for Abatacept (Orencia) for Intravenous Infusion**

Regions: ☒ **Texas** ☐ **Florida** ☐ **Indiana** ☐ **New Jersey** ☒ **New Mexico**

**Impacted Areas:**

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

**Available LCD/NCD/LCA: None**

**Disclaimer:**

WellMed Coverage Determination Policies are developed as needed, are regularly reviewed and updated, and are subject to change. They represent a portion of the resources used to support WellMed coverage decision making. WellMed may modify these Policy Guidelines at any time. Medicare source materials used to develop these guidelines include, but are not limited to, CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Medicare Benefit Policy Manual, Medicare Claims Processing Manual, Medicare Program Integrity Manual, Medicare Managed Care Manual, etc. The information presented in the WellMed Coverage Determination Policies is believed to be accurate and current as of the date of publication, and is provided on an "AS IS" basis. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

Doctors helping patients for more than 25 years

**Title: Coverage Determination Policy for Abatacept (Orencia) for Intravenous Infusion**

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**Coverage Policy Number: 015.005**

**Line of Business:** Medicare Part B

**Policy Type:** Prior Authorization

## Coverage Determination:

This policy refers to abatacept injection for intravenous infusion only. Abatacept for subcutaneous administration is excluded from Medicare Part B coverage since it is on the self-administered drug exclusion list. (LCA A53127 & A52571)[22] Generally, requests for subQ Abatacept should be directed to the member's pharmacy benefit.

**PLEASE NOTE**: All requests for IV abatacept must include justification as to why IV route is medically reasonable and necessary. Medicare rules expect that if a patient is clinically able to self-administer a drug and there is no clear medical justification to do otherwise, then the patient must either self-administer that drug or self-pay for the alternative. For example, an individual afflicted with paraplegia or advanced dementia would not have the capacity to self-administer any injectable drug. Medicare considers the following factors to be unrelated to medical decision making: 1. Patient convenience, 2. Patient co-pays and financial liability. See the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals at http://www.cms.hhs.gov/manuals/Downloads/bp102c15.pdf.

**For ALL indications:**

Patient must not be receiving abatacept in combination with either of the following:

1. Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)][5]
   OR
   Janus kinase inhibitor [e.g., Xeljanz (tofacitinib), Olumiant (barticitinib)]
2. Patients must be screened for latent TB infection prior to initiating therapy. Patients testing positive should be treated prior to initiating Orencia[5]
3. Patients should be screened for viral hepatitis prior to initiating Orencia

## Initial/New Requests

**Abatacept is proven and medically necessary for:**

1. **Rheumatoid arthritis**, when ALL of the following criteria are met:
   a. Diagnosis of moderately to severely active rheumatoid arthritis (RA)
   b. Abatacept is initiated and titrated according to US FDA labeled dosing for rheumatoid arthritis up to a maximum of (or equivalent dose and interval schedule).

2. **Psoriatic arthritis**, when ALL of the following criteria are met:
   a. Diagnosis of active psoriatic arthritis (PsA);
   b. Abatacept is initiated and titrated according to US FDA labeled dosing for psoriatic arthritis up to a maximum of (or equivalent dose and interval schedule).

3. **Polyarticular juvenile idiopathic arthritis,** when ALL of the following criteria are met:
   a. Diagnosis of moderately to severely active polyarticular juvenile idiopathic arthritis (PJIA)
   b. Abatacept is initiated and titrated according to US FDA labeled dosing for polyarticular juvenile idiopathic arthritis up to a maximum of (or equivalent dose and interval schedule).

4. **Prophylaxis for Acute graft-versus-host disease (aGVHD), when ALL of the following criteria are met:**
   a. Patient is at least 2 years old
   b. Patient is undergoing hematopoietic stem cell transplantation (HSCT) from a matched donor or from 1 allele-mismatched unrelated donor
   c. Patient is receiving Orencia in combination with a calcineurin inhibitor (e.g. cyclosporine, tacrolimus)
   d. Patient is receiving Orencia in combination with methotrexate
   e. Authorization is for no more than 4 doses (refer to FDA approved dosing section below)

5. **Treatment of chronic graft-versus-host disease (GVHD) when all of the following criteria are met:**
   a. Diagnosis of steroid-refractory chronic GVHD; and
   b. One of the following:
   - Patient is receiving Orencia in combination with systemic corticosteroids OR
   - Patient is intolerant to systemic corticosteroid therapy

6. **Treatment of immune checkpoint inhibitor-related toxicities when all of the following criteria are met**
   a. Patient has recently received checkpoint inhibitor therapy [e.g., Keytruda (Pembrolizumab), Opdivo (Nivolumab)]
   b. Diagnosis of severe (G3) or life threatening (G4) immunotherapy-related myocarditis, pericarditis, arrhythmias, or impaired ventricular function, or conduction abnormalities
   c. No improvement of toxicity within 24 hours of starting pulse-dose methylprednisolone
   d. History of failure, contraindication, or intolerance to infliximab (e.g., Inflectra, Remicade)
   e. Authorization is for no more than 4 doses

## Renewal/Continuation of Therapy Requests

- For all approved indications, ALL of the following must be met:
  1. Documentation of positive clinical response
  2. Dose is in accordance to FDA labeled dosing for indication
  3. Patient is not receiving abatacept in combination with either of the following:
     a. Biologic DMARD [e.g., Enbrel (etanercept), Humira (adalimumab), Cimzia (certolizumab), Simponi (golimumab)]
     b. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]

- For chronic graft-versus-host disease (GVHD), all of the following must be met:
  1. Documentation of positive clinical response
  2. Patient continues to experience chronic GVHD
  3. One of the following:
     a. Patient is receiving Orencia in combination with systemic corticosteroids
     b. Patient is intolerant to systemic corticosteroid therapy
     c. Patient has been successfully tapered off of corticosteroid therapy

Abatacept is **unproven and NOT medically necessary** for the treatment of:

1. Multiple sclerosis
2. Systemic lupus erythematosus
3. Uveitis associated with Behcet's disease

## FDA Approved Dose and Indications

| FDA approved indications | Approved Dosing |
|---|---|
| Rheumatoid Arthritis<br>Psoriatic Arthritis | • 500mg IV week 0, 2, 4 then every 4 weeks for patients <60kg<br>• 750mg IV week 0, 2, 4 then every 4 weeks for patients 60kg- 100kg<br>• 1,000mg IV week 0, 2, 4 then every 4 weeks for patients >100kg |
| Polyarticular Juvenile idiopathic arthritis | • 10 mg/kg IV for <75kg<br>• Administer the adult dosing (RA dosing above) for those weighing ≥75kg (not to exceed a maximum dose of 1,000mg) |
| Acute graft-versus-host disease - Prophylaxis | • 10 mg/kg IV the day before transplantation (Day -1) and on Days 5, 14, and 28 after transplantation; MAX dose, 1000 mg |

**NOTE: For Acute graft-versus-host disease Prophylaxis:**

Prior to initiation, administer antiviral prophylactic treatment for Epstein-Barr virus reactivation, and continue for 6 months following hematopoietic stem cell transplantation (HSCT). Additionally, consider prophylactic antivirals for cytomegalovirus (CMV) infection/reactivation during treatment and for 6 months following HSCT

## General Background:

Orencia® (abatacept) is a fully human, soluble, fusion protein, selective co-stimulation modulator which inhibits T lymphocyte activation by binding to CD80 and CD86, thereby blocking interaction with CD28. This interaction provides a costimulatory signal necessary for full activation of T lymphocytes.

Abatacept is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis. Abatacept may be used as monotherapy or concomitantly with DMARDs other than tumor necrosis factor (TNF) antagonists. Abatacept is also indicated for reducing signs and symptoms in pediatric patients 6 years of age and older with moderately to severely active polyarticular juvenile idiopathic arthritis. Abatacept may be used as monotherapy or concomitantly with methotrexate. Abatacept is also indicated for the treatment of adult patients with active psoriatic arthritis.

The labeling for Abatacept states that it should not be administered concomitantly with TNF antagonists or with other biologic RA therapy, such as Kineret (anakinra), an interleukin-1 receptor antagonist. In controlled clinical trials in patients with adult RA, patients receiving concomitant Abatacept and TNF antagonist therapy experienced more infections (63%) and serious infections (4.4%) compared to patients treated with only TNF antagonists (43% and 0.8%, respectively). These trials failed to demonstrate superiority of results with concomitant administration of Abatacept and TNF antagonists. Therefore, clinical evidence does not support concurrent therapy with Abatacept and TNF antagonists.

Medicare does not have a National Coverage Determination (NCD) that addresses abatacept. Local Coverage Determinations (LCDs) do not exist at the time of revision of this policy. Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. See the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals at http://www.cms.hhs.gov/manuals/Downloads/bp102c15.pdf and Local Coverage Article: Self-Administered Drug Exclusion List (A53127).

## Clinical Evidence:

**Rheumatoid Arthritis**

A randomized, multicenter, active controlled Phase 3b trial, the Assessing Very Early Rheumatoid arthritis treatment (AVERT) trial (n=351) of 24 months, with a 12-month, double-blind treatment period, evaluated clinical remission with subcutaneous abatacept plus methotrexate (MTX) and abatacept monotherapy in patients with early rheumatoid arthritis (RA), and maintenance of remission following the rapid withdrawal of all RA treatment. During the 12 month treatment period, patients were randomized (1:1:1) to receive abatacept plus MTX (n=119), abatacept monotherapy (n=116), or MTX monotherapy (n=116), stratified by corticosteroid use at baseline. Patients with a Disease Activity Score (DAS)28 (CRP) <3.2 at month 12 could enter the 12 month withdrawal period where abatacept was immediately stopped and MTX and steroids tapered over 1 month. Patients with DAS28 ≥ 3.2 discontinued the study. After month 15, patients in the withdrawal period who experienced a flare could re-start open label SC abatacept 125mg plus MTX. Coprimary endpoints were the proportion of randomized and treated patients in DAS-defined remission (CRP 5 <2.6) at month 12 and months 12 and 18 for abatacept plus MTX versus MTX. For the abatacept plus MTX versus MTX, DAS28 (CRP) < 2.6 was achieved in 60.9% versus 45.2% (p=0.010) at 12 months, and following treatment withdrawal, in 14.8% versus 7.8% (p=0.045) at both 12 and 18 months. DAS28 (CRP) <2.6 was achieved for abatacept monotherapy in 42.5% (month 12) and 12.45% (both months 12 and 18). Both abatacept arms had a safety profile comparable to MTX alone. The authors concluded that abatacept plus MTX demonstrated efficacy compared with MTX alone in early RA, with a comparable safety profile to MTX. Abatacept achieved some sustained remission following withdrawal of all RA therapy in the respective groups.

The 2015 American College of Rheumatology (ACR) RA treatment guideline addresses the use of DMARDS, biologics, tofacitinib, and glucocorticoids in early (<6 months) and established (≥ 6 months) RA and the use of various treatment approaches in frequently encountered clinical scenarios, including treat-to-target, switching between therapies, tapering of therapy, the use of biologics and DMARDs in high-risk RA patients, vaccination in patients with RA receiving DMARDs or biologics, TB screening with biologics or tofacitinib, and laboratory monitoring with DMARDs. The guideline recommendations apply to common clinical situations, since the panel considered issues common to most patients, not exceptions. Recommendations are classified as either strong or conditional. A strong recommendation means that the panel was confident that the desirable effects of following the recommendation outweigh the undesirable effects (or vice versa), so the course of action would apply to most patients, and only a small proportion would not want to follow the recommendation. A conditional recommendation means that the desirable effects of following the recommendation probably outweigh the undesirable effects, so the course of action would apply to the majority of patients, but some may not want to follow the recommendation. As a result, conditional recommendations are preference sensitive and warrant a shared decision-making approach.

**Psoriatic Arthritis**

A randomized, placebo controlled Phase 3 trial assessed the efficacy and safety of abatacept in adult patients (>18 years old) with psoriatic arthritis. Patients were randomly assigned in a double-blind manner to receive either subcutaneous abatacept 125mg weekly or placebo for 24 weeks. Patients who had not achieved ≥ 20% improvement in swollen and tender joint counts from baseline to week 16 were switched to open-label abatacept weekly for 28 weeks. At the end of the open-label period, patients had the option of entering a 1-year, long-term extension. Primary efficacy endpoint was the proportion of patients with ACR20 responses at week 24. Abatacept significantly increased ACR20 response versus placebo at week 24 (39.4% vs 22.3%; p<0.001). Although abatacept numerically increased Health Assessment Questionnaire–Disability Index response rates (reduction from baseline ≥0.35) at week 24, this was not statistically significant (31.0% vs 23.7%; p=0.097). The benefits of abatacept were seen in ACR20 responses regardless of TNF inhibitor exposure and in other musculoskeletal manifestations, but significance could not be attributed due to ranking below Health Assessment Questionnaire–Disability Index response in hierarchical testing. The benefit on psoriasis lesions was modest. Efficacy was maintained or improved up to week 52. Abatacept was well tolerated with no new safety signals. The authors concluded that abatacept treatment of PsA in achieved its primary end point, ACR20 response, showed beneficial trends overall in musculoskeletal manifestations and was well tolerated. There was only a modest impact on psoriasis lesions.

**Polyarticular Juvenile Idiopathic Arthritis**

The long-term extension (LTE) phase of a pivotal phase III study examining the efficacy and safety of abatacept in patients with juvenile idiopathic arthritis (JIA) reported the efficacy and safety outcomes of treatment (up to 10mg/kg every 4 weeks), with or without non-biologic DMARDs, for up to 7 years of followup. One hundred fifty-three of 190 patients (80.5%) entered the LTE phase, with only 69 patients (36.3%) completing the study. The overall incidence rate (events per 100 patient-years) of adverse events decreased from 433.61 events during the short-term phase compared to 132.39 events during the LTE phase. Serious adverse events (6.82 vs. 5.60), malignancies (1.12 vs. 0), and autoimmune events (2.26 vs. 1.18) also were reduced. Serious infections were slightly increased (1.13 vs. 1.72). American College of Rheumatology (ACR) Pediatric 30 (Pedi 30), Pedi 70, responses, and clinically inactive disease status were maintained throughout the extension phase in those patients continuing to receive therapy. Improvements in the Child Health Questionnaire summary scores were also maintained over the course of the study. The authors concluded that long-term abatacept therapy, for up to 7 years, was associated with consistent safety, efficacy, and quality of life benefits in patients with JIA. The 2011 American College of Rheumatology (ACR) Recommendations for the Treatment of Juvenile Idiopathic Arthritis include abatacept for certain clinical scenarios.

**Prophylaxis of Acute Graft versus Host Disease**

In a multicenter, two cohort clinical study (GVHD-1, NCT01743131), abatacept, in combination with a calcineurin inhibitor (CNI) and methotrexate (MTX), was evaluated in patients age 6 years and older who underwent hematopoietic stem cell transplantation (HSCT) from a matched or 1 allele-mismatched unrelated donor. The two cohorts included an open-label, single-arm study for 43 patients who underwent a 7 of 8 Human Leukocyte Antigen (HLA)-matched HSCT (7 of 8 cohort) and 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 CNI and MTX (8 of 8 cohort). In both the 7/8 and 8/8 cohorts, abatacept 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. Abatacept plus CNI and MTX did not significantly improve grade III-IV GFS versus placebo plus CNI and MTX at Day 180 posttransplantation. In the 8/8 cohort, the efficacy of abatacept plus CNI and MTX at Day 180 post-transplantation for grade III-IV GFS rate and hazard ratio, grade II-IV GFS rate and hazard ratio, and OS rate and hazard ratio were 87% and 0.55, 50% and 0.54, and 97% and 0.33, respectively. In the placebo plus CNI and MTX, the efficacy results at Day 180 post-transplantation for grade III-IV GFS rate, grade II-IV GFS rate, and OS rate were 75%, 32%, and 84%, respectively. In an exploratory analysis of the 7/8 cohort of abatacept-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%, 53%, and 98%, respectively.

The GVHD-2 study was a clinical study that used data from the Center for International Blood and Marrow Transplant Research (CIBMTR).32 The study analyzed outcomes of abatacept in combination with a CNI and MTX, versus a CNI and MTX 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 abatacept plus CNI and MTX-treated group (n=54) included 42 patients from GVHD-1, in addition to 12 patients treated with abatacept outside of GVHD-1. The comparator group (n=162) was randomly selected in a 3:1 ratio to the abatacept-treated group from the CIBMTR registry from patients who had not received abatacept 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 OS at Day 180 post-HSCT. The OS rate at Day 180 in the abatacept plus CNI and MTX group was 98% and the OS rate at Day 180 in the CNI and MTX group was 75%.

**NCCN Recommended Uses**

According to the NCCN Drugs & Biologics Compendium, NCCN recommends (2A) abatacept for the treatment of:

- Chronic graft-versus-host disease (GVHD) as additional therapy in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options
- Immune checkpoint inhibitor-related toxicities - Consider adding abatacept for the management of immunotherapy-related:
  Severe (G3) or life-threatening (G4) myocarditis, pericarditis, arrhythmias, impaired ventricular function, or conduction abnormalities if no improvement within 24 hours of starting pulse-dose methylprednisolone

## HCPCS **Code**:

| HCPCS Code: | Description: |
|---|---|
| J0129 | Injection, Abatacept (Orencia), 10mg |

## Acronyms:

TNF = tumor necrosis factor; NCD = National Coverage Determination; LCD = Local Coverage Determinations; RA = rheumatoid arthritis; PsA = psoriatic arthritis; DMARD = disease-modifying antirheumatic drug; FDA = Food and Drug Administration; PJIA = polyarticular juvenile idiopathic arthritis; ACR = American College of RheumatologyDMARD – Disease Modifying Anti-Rheumatic Drug; GVHD - Graft versus host disease; PsA - active psoriatic arthritis; TNF - tumor necrosis factor; RA – Rheumatoid Arthritis; ACR – American College of Rheumatology; PJIA - Polyarticular Juvenile Idiopathic Arthritis**;** (aGVHD) - Acute graft versus host disease; HSCT - Hematopoietic stem cell transplantation; calcineurin inhibitor – CNI; methotrexate –MTX; overall survival – OS; aGVHD free survival – GFS; Human Leukocyte Antigen - HLA

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