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Abatacept (Orencia) Clinical Guideline for Home Intravenous Therapy

Section: Clinical Guideline
Compliance: ACHC Infusion Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
Policy ID: CG027
Effective: 6/1/2022
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Approved by, Title and Date Approved: Kathleen Patrick, President 6/1/22, 6/1/25

I. BACKGROUND

Abatacept (Orencia) is a combination of the extracellular domain of human cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) linked to the modified heavy chain portion of human immunoglobulin G1 (IgG1). Abatacept binds to CD80 and CD86 receptors on the antigen-presenting cell and prevents them from binding to CD28 on the T cell for optimal T cell activation. Thus, it is a biological response modifier that demonstrates anti-inflammatory effects by downregulating T cell activation. Abatacept is indicated for the treatment of moderate to severe rheumatoid arthritis (RA) in adult patients, active polyarticular juvenile idiopathic arthritis (pJIA), active psoriatic arthritis (PsA) in pediatric and adult patients, and for the prophylaxis of acute graft versus host disease (aGVHD), in combination with a calcineurin inhibitor and methotrexate, in adults and pediatric patients undergoing hematopoietic stem cell transplantation. The following outlines the procedures for servicing patients in need of outpatient abatacept home infusions.

II. PATIENT ACCEPTANCE CRITERIA

A. All candidates for home care service must be evaluated by the clinician(s) and deemed appropriate to receive home care based upon CarepathRx admission criteria:

B. The decision to administer a first dose in the home by a field nurse will be determined on a case-by-case basis and reviewed by nursing and pharmacy management. The following criteria will be evaluated:

1. Prescriber preference
2. Allergy profile
3. Age
4. Other relevant social and/or medical history

C. Physician orders for abatacept must include:

1. Patient weight
2. Drug and dose (including weight-based dosage)
3. Route of administration
4. Frequency of administration
5. Emergency medications per protocol
6. Orders for pre-medications
7. Line care protocol

8. Routine lab monitoring, if applicable

D. Baseline labs prior to starting therapy

1. Tuberculosis screening
2. Viral hepatitis screening (Hepatitis B)
3. EBV status prior to hematopoietic stem cell transplantation

E. Dispensing pharmacy treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient-specific orders are provided by physician. See Appendix A (Nursing CarepathRx policy on *Management of Allergic/Anaphylactic Reactions*).

III. PHARMACOLOGIC OVERVIEW

Refer to manufacturer's full Prescribing Information for most up to date information

A. Indications

1. Adult patients with moderately to severely active rheumatoid arthritis (RA) or active psoriatic arthritis (PsA)
2. Patients 2 years of age and older with active psoriatic arthritis (PsA)
3. Patients 2 years of age and older with moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA)
4. Prophylaxis of acute graft versus host disease (aGVHD), in combination with a calcineurin inhibitor and methotrexate, in adults and pediatric patients 2 years of age and older undergoing hematopoietic stem cell transplantation (HSCT) from a matched or 1 allele-mismatched unrelated donor

B. Dosing
**Subcutaneous dosing and administration will not be discussed in the scope of this guideline*

1. Adults

a. Intravenous Use for Adult RA and Adult PsA
Administer at 0, 2, and 4 weeks, and every 4 weeks thereafter, as a 30-minute infusion per these weight-based recommendations:

Body Weight of Patient	Dose	Number of Vials
Less than 60 kg	500 mg	2
60 to 100 kg	750 mg	3
More than 100 kg	1000	4

Prior to the first subcutaneous dose, may administer an optional loading dose as a single intravenous infusion as per body weight categories above.

b. Intravenous Use for prophylaxis of aGVHD
10 mg/kg dose (maximum dose 1,000 mg) as a 60-minute infusion on the day before transplantation, followed by a dose on Day 5, 14, and 28 after transplant.

2. Pediatrics

   a. Intravenous Use for pJIA in Pediatric Patients ≥6 Years Old

      Pediatric patients weighing <75 kg administer 10 mg/kg intravenously and those weighing ≥75 kg administer the adult intravenous dosing regimen (not to exceed a maximum dose of 1,000 mg), as a 30-minute infusion.

      Subsequently administer infusions at 2 and 4 weeks and every 4 weeks thereafter.

   b. Intravenous Use for prophylaxis of aGVHD

      For patients 6 years and older, administer at a 10 mg/kg dose (maximum dose 1,000 mg) as a 60-minute infusion on the day before transplantation, followed by a dose on Day 5, 14, and 28 after transplant.

      For patients 2 to less than 6 years old, administer a 15 mg/kg dose as a 60 minute infusion on the day before transplantation, followed by a 12 mg/kg dose as a 60-minute infusion on Day 5, 14, and 28 after transplant.

* Dosing is based off actual body weight. Abatacept has not been studied in extremes of body weights.

C. Dose Adjustment: No dosage adjustment is recommended in patient with renal or hepatic impairment.

D. Duration: Duration of therapy should be dependent on patient response and adverse reactions.

E. Contraindications: None

F. Warnings and Precautions:

1. **Hypersensitivity reactions**: hypersensitivity and anaphylaxis have occurred. In clinical trials with adult RA patients, other hypersensitivity reactions included hypotension, urticaria, and dyspnea. In post-marketing experience, there have been incidences of anaphylaxis and severe angioedema. Angioedema has occurred with the first and subsequent doses and has occurred within hours to days of administration.

2. **Increased risk of infection:** Serious infections, including sepsis and pneumonia, have been reported in patients receiving abatacept. Many of the serious infections have occurred in patients on concomitant immunosuppressive therapy which in addition to their underlying disease, could further predispose them to infection. A higher rate of serious infections has been observed in adult RA patients treated with concurrent TNF antagonists and abatacept compared to those treated with abatacept alone. Healthcare providers should exercise caution when considering the use of abatacept in patients with a history of recurrent infections, underlying conditions which may predispose them to infections, or chronic, latent, or localized infections. Patients who develop a new infection while undergoing treatment with abatacept should be monitored closely. Administration of abatacept should be discontinued if a patient develops a serious infection.

a. Tuberculosis: Prior to initiating abatacept, patients should be screened for latent tuberculosis (TB) infection according to current TB guidelines. Patients testing positive in TB screening should be treated by standard medical practice prior to therapy with abatacept.
b. Viral hepatitis: Antirheumatic therapies have been associated with hepatitis B reactivation. Therefore, screening for viral hepatitis should be performed in accordance with published guidelines before starting abatacept.
c. Increased Risk of Infection with Concomitant Use of TNF Antagonists, Other Biologic RA/PsA Therapy, or JAK Inhibitors: In controlled clinical trials in patients with adult RA, patients receiving concomitant intravenous abatacept and TNF antagonist therapy experienced more infections (63% vs. 43%) and serious infections (4.4% vs. 0.8%) compared to patients treated with only TNF antagonists. Concurrent therapy with abatacept and a TNF antagonist is not recommended. While transitioning from TNF antagonist therapy to abatacept, patients should be monitored for signs of infection. Additionally, concomitant use of abatacept with other biologic RA/PsA therapy or JAK inhibitors is not recommended.
d. Cytomegalovirus (CMV) and Epstein-Barr Virus (EBV) reactivation has occurred in patients treated for aGVHD prophylaxis: Post-Transplant Lymphoproliferative Disorder (PTLD) occurred in patients who received abatacept for aGVHD prophylaxis during unrelated HSCT. Of 116 patients who received abatacept, 4 patients (3.4%) experienced PTLD. All the PTLD events were associated with Epstein-Barr virus (EBV) infection. Monitor patients for EBV reactivation in accordance with institutional practices. Provide prophylaxis for EBV infection for 6 months post-transplantation to prevent EBV-associated PTLD. Cytomegalovirus (CMV) invasive disease occurred in patients who received abatacept for aGVHD prophylaxis during unrelated HSCT. Of 116 patients who received abatacept, 7% experienced CMV invasive diseases up to day 225 post-transplant. All the patients who experienced CMV invasive disease were CMV serology positive at baseline. The median time to onset of the event was 91 days post-transplant. CMV invasive diseases predominantly involved the gastrointestinal tract. Monitor patients for CMV infection/reactivation for 6 months post-transplant regardless of the results of donor and recipient pre-transplant CMV serology. Consider prophylaxis for CMV infection/reactivation

3. **Immunizations:** Live vaccines should not be given concurrently or within 3 months of discontinuation. Prior to initiating in pediatric and adult patients, update vaccinations in accordance with current vaccination guidelines. Abatacept-treated patients may receive current non-live vaccines. Live vaccines should not be given concurrently with abatacept or within 3 months after discontinuation.

4. **Increased Risk of Adverse Reactions When Used in Patients with Chronic Obstructive Pulmonary Disease (COPD):** Adult COPD patients treated with abatacept for RA developed adverse reactions more frequently than those treated with placebo, including COPD exacerbations, cough, rhonchi, and dyspnea. A greater percentage of patients treated with abatacept developed a serious adverse event compared to patients treated with placebo. Use of abatacept in patients with COPD should be undertaken with caution and such patients should be monitored for worsening of their respiratory status.

5. **Immunosuppression:** The possibility exists for drugs inhibiting T-cell activation, including abatacept, to affect host defenses against infections and malignancies since T

cells mediate cellular immune responses. In clinical trials in patients with adult RA, a higher rate of infections was seen in abatacept-treated patients compared to placebo-treated patients. The impact of treatment with abatacept on the development and course of malignancies is not fully understood. There have been reports of malignancies, including skin cancer in patients receiving abatacept. Periodic skin examinations are recommended for all abatacept-treated patients, particularly those with risk factors for skin cancer.

6. **Pregnancy and Lactation**: There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to abatacept during pregnancy. Healthcare professionals are encouraged to register patients, and pregnant women are encouraged to enroll themselves by calling 1-877-311-8972. The data with abatacept use in pregnant women are insufficient to inform on drug-associated risk. However, there are clinical considerations for administering live vaccines to infants who were exposed to abatacept while in utero. In reproductive toxicology studies in rats and rabbits, no fetal malformations were observed with intravenous administration of abatacept during organogenesis at doses that produced exposures approximately 29 times the exposure at the maximum recommended human dose (MRHD) of 10 mg/kg/month on an AUC basis. However, in a pre and postnatal development study in rats, abatacept altered immune function in female rats at 11 times the MRHD on an AUC basis. There are no adequate and well-controlled studies of abatacept use in pregnant women. The data with abatacept use in pregnant women are insufficient to inform on drug-associated risk.

    a. Lactation: There is no information regarding the presence of abatacept in human milk, the effects on the breastfed infant, or the effects on milk production. However, abatacept was present in the milk of lactating rats dosed with abatacept.

G. Pharmacokinetics

1. Vd, IV administration: 0.07 L/kg
2. Metabolized by proteolytic enzymes into smaller peptides and amino acids.
3. Elimination half-life for IV administration: 13 days
4. Clearance, IV: 0.22 mL/hr/kg

H. Adverse Reactions

1. Most common adverse reactions (≥10%) in RA and PsA

    a. Headache
    b. Upper respiratory tract infection
    c. Nasopharyngitis
    d. Nausea

2. Most common adverse reactions (≥ 5%) in patients with pJIA

    a. Upper respiratory tract infection
    b. Nasopharyngitis
    c. Headache
    d. Nausea
    e. Diarrhea

f. Cough
g. Pyrexia
h. Abdominal pain

3. Most common adverse reactions (≥10%) in prophylaxis of aGVHD

a. Anemia
b. Hypertension
c. CMV reactivation/CMV infection
d. Pyrexia
e. Pneumonia
f. Epistaxis
g. CD4 lymphocyte decrease
h. Hypermagnesemia
i. Acute kidney injury

I. Drug Interactions:

1. Avoid concurrent use of abatacept with these immunosuppressive medications due to increased risk for infection: biologics, anifrolumab, and Janus Kinase Inhibitors (JKI's)
2. Live vaccines: administration of live vaccines during or within 3 months following abatacept treatment is not recommended.
3. Blood glucose testing: When receiving intravenous abatacept, patients that require blood glucose monitoring should be advised to consider methods that do not react with maltose, such as those based on glucose dehydrogenase nicotine adenine dinucleotide (GDH-NAD), glucose oxidase, or glucose hexokinase test methods. The GDH-PQQ based glucose monitoring systems may react with the maltose present in abatacept for intravenous administration, resulting in falsely elevated blood glucose readings on the day of infusion
4. Drug-drug interactions may exist. Consult interaction database for patient specific assessment.

IV. ADMINISTRATIVE GUIDELINES

A. Administration- IV infusions should be given immediately after reconstitution and dilution. Begin infusion within 4 hours of preparation per current USP Immediate-Use Guidelines.

B. Abatacept must be reconstituted and prepared using only a **silicone-free disposable syringe** that is provided with each vial.

C. Utilize a **0.2 to 1.2-micron in-line or add on filter** during intravenous administration.

D. Do not co-administer with other products in the same IV line.

V. NURSING PROCEDURES

A. Supplies include but are not limited to:

1. Alcohol Swabs

2. Gloves
3. Tape
4. Peripheral IV access supplies for patients requiring peripheral IV access
    a. IV start Kit
    b. Peripheral IV catheter (ex. 22 Gauge x1" and 24 Gauge x ¾")
    c. Extension set 8" with needless connector
5. Port access supplies for patients with a port
    a. Port needle (ex. 22 Gauge x ¾ to 1" safe step)
    b. Needless connector
    c. Central line dressing change kit
6. IV Pole
7. IV administration set (flow regulator [ex: dial-a-flow] or gravity) with in-line or add-on 0.22-1.2-micron filter
8. Syringes (10-50 mL) for removal of excess diluent from stock bag
9. Needles (20 G x 1")
10. Sharps container

B. Prescription Items

1. Vials of abatacept with <u>silicone free syringes</u>
2. Sterile Water for Injection (SWFI) vials
3. Sodium chloride 0.9% 100 mL stock bag
4. Standard flushes per protocol
5. Anaphylaxis kit per protocol

C. How Supplied

Abatacept for infusion is supplied as a white lyophilized powder for intravenous infusion after reconstitution and dilution. It is supplied as 250mg vials **with each vial set also containing a <u>silicone free syringe</u>.**

D. Storage and Handling: store lyophilized powder in vials in the refrigerator at 36 °F to 46 °F (2 °C to 8 °C) until ready to use. Be sure to keep in the original package and out of the light. DO NOT freeze.

E. Compatibility: Stable in 0.9% Sodium Chloride.

F. Procedures:

1. Explain the reasoning for visit and use of abatacept
2. Don gloves.
3. Assess for signs and symptoms of infection prior to establishing venous access and preparing medication.
4. Establish venous access prior to preparation of drug
5. Counsel patient on warnings, precautions, and potential side effects including but not limited to: infection, nausea, diarrhea, abdominal pain, anemia, and hypertension.
6. Prepare the product

    a. Use only a **<u>silicone-free disposable syringe</u>** and an 18- to 21-gauge needle to reconstitute the 250 mg vial of lyophilized abatacept powder with 10 mL of sterile water for injection to a concentration of 25 mg/mL. A silicone-free disposable

syringe is provided with the vial of lyophilized powder. If dropped or contaminated, information on obtaining additional silicone-free disposable syringes may be obtained at 1-800-ORENCIA. If the vial of lyophilized powder is inadvertently reconstituted using a siliconized syringe, discard solution

b. Gently swirl the vial to minimize foam formation, until the contents are completely dissolved. Do not shake. Avoid prolonged or vigorous agitation. Upon complete dissolution of the lyophilized powder, vent the vial with a needle to dissipate any foam that may be present
c. Visually inspect the reconstituted solution (the solution should be clear and colorless to pale yellow). Do not use if opaque particles, discoloration, or other foreign particles are present.
d. From a 100 mL infusion bag of 0.9% sodium chloride, withdraw a volume equal to the volume of reconstituted solution required for the patient's dose and discard. A silicone syringe may be used to draw up the diluent that is to be discarded.
e. Slowly add the reconstituted abatacept solution from the vial into the infusion bag using **the same silicone-free disposable syringe** used during reconstitution. Gently mix; do not shake the bag or bottle
f. The final concentration should be no more than 10 mg/mL. Discard any vials with excess drug not needed for the infusion.

7. Infusion rates:
   a. Infuse over 30 minutes for psoriatic arthritis, rheumatoid arthritis, and pJIA indications
   b. Infuse over 60 minutes for acute graft-versus-host disease prophylaxis.

8. Post infusion monitoring: Monitor patient and vital signs periodically during the infusion and 30 minutes after the infusion is complete per CarePathRx Nursing Best Practice Administration Guidelines.

VI. CLINICAL MONITORING

A. Prior to therapy

1. Baseline laboratory testing (CBC with differential, CMP)
2. Tuberculosis screening
3. Viral hepatitis screening (Hepatitis B)
4. EBV status prior to hematopoietic stem cell transplantation
5. No active infections

B. During therapy

1. Monitor for signs/symptoms of infection
2. Monitor for hypersensitivity reactions
3. Perform periodic skin examinations and monitor for malignancies
4. In patients receiving abatacept for prophylaxis of acute graft-versus-host disease following hematopoietic stem cell transplant monitor for:
   a. Cytomegalovirus infection/reactivation
   b. Epstein-Barr virus reactivation
   c. Post-transplant Lymphoproliferative Disorder
5. Abatacept may result in a falsely elevated blood glucose measurement due to assay

interference with the glucose dehydrogenase pyrroloquinoline quinone (GDH-PQQ) method.

6. Monitor for efficacy:
   a. RA, pJIA, PsA: joint stiffness, tenderness, joint pain and aches, joint swelling, fatigue, rash or patches of scaly skin (PsA).
   b. aGVHD: nausea, vomiting, diarrhea, abdominal pain, cramps, jaundice, skin irritation, rash. Acute GVHD can occur days and up to 6 months after transplant.

Please refer to the package insert for the most up to date guidance on this medication.

REFERENCES:

Orencia [package insert]. Princeton, NJ. Bristol-Myers Squibb Company. 2023.

United States Pharmacopeia (USP). General Chapter, <797> Pharmaceutical Compounding—Sterile Preparations. (2023) USP-NF. Rockville, MD: United States Pharmacopeia. Accessed November 29, 2023.

APPENDIX A: ANAPHYLAXIS KIT INTRUCTIONS

Emergency Medication After Your Infusion

Please call your pharmacy if you have any questions or concerns. In the event of an emergency, always call 911.

Your nurse will tell you when you need to use Emergency Medications.
The epinephrine dose will be noted on the Anaphylaxis Protocol included with your kit.

Start with a clean work surface and clean hands.

Open the supply bag labeled Anaphylaxis Kit Contents.

You will need:

1. **Bag containing Pills** (2 Acetaminophen and 2 Diphenhydramine)
2. **Bag containing Alcohol Prep Pads**
3. **Bag labeled IM Epinephrine**

All other contents will not be needed.

Open the IM Epinephrine Bag

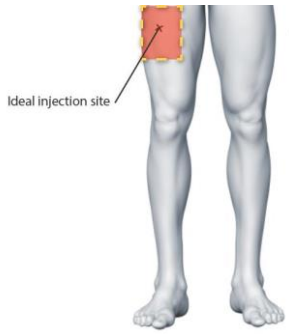
1. **Remove 1 of each item**
    a. 1 -syringe
    b. 1 – brown labeled filter needle (BD Filter Needle)- **for ampule use only**
    c. 1 – black labeled safety needle (Magellan Hypodermic Safety Needle 22G x 1”)
    d. 1 ampule of epinephrine

Prepare IM (intramuscular) injection of Epinephrine:

1. **Attach the brown filtered needle to syringe**
    a. Be careful to not touch the tip of the syringe or the needle.
2. Using an **alcohol swab, wipe the neck of the epinephrine ampule.**
3. Holding the ampule upright, **swirl and flick the ampule until all fluid flows to the bottom chamber** (the top chamber should be empty).
4. Using a new alcohol wipe, grasp the neck of the ampule and with your other hand grasp the bottom chamber of the ampule. **Quickly snap the top of the ampule off, directing the snap way from you.**
5. **Place the tip of the brown filter needle inside the ampule**. Tilting the ampule, **withdraw dose of medication into the syringe** by gently pulling back on the plunger. Be careful to not pull the plunger out of the syringe.
6. Remove the needle from the ampule and h**old the syringe upright** with the needle pointing upward. **Gently tap the side of the syringe to bring any air to the top of the syringe.**
7. **Push the air out of the syringe by gently pushing on the plunger**.
8. Replace the cap on the brown filter needle. Discard remainder in ampule.

9. **Remove the brown filter needle and place the black safety needle onto the syringe.**

Give your IM Epinephrine injection



1. **Grasp your leg muscle at the outer mid-thigh** and **cleanse the area** with a new alcohol wipe.
2. **Push the needle into your leg muscle straight** in at a 90-degree angle.
3. **Inject the medication** by depressing the plunger in a slow and steady motion.
4. **Remove the needle** and wipe the site with the alcohol wipe.
5. May repeat dose every 5 minutes (**maximum 3 doses**) if ordered per protocol.

Take the pills by mouth.

a. 2 – Acetaminophen
b. 2 – Diphenhydramine

Place all trash in the bag the pills came in and take with you when you seek medical care. **Give the bag to the nurse or EMT**, so your doctor will know what medication you already took. They will properly dispose of the syringe and needles.

Call 911 or have someone drive you to the emergency department.