Abatacept (ab a TA sept)

Medication Safety Issues
Sound-alike/look-alike issues:
Orencia may be confused with Oracea
Brand Names: US Orencia
Brand Names: Canada Orencia
Index Terms BMS-188667; CTLA-4Ig
Generic Availability (US) No
Pharmacologic Category Antirheumatic, Disease Modifying; Selective T-Cell Costimulation Blocker
Use
Rheumatoid arthritis: Treatment of moderately to severely active adult rheumatoid arthritis (RA); may be used as monotherapy or in combination with other DMARDs
Note: Abatacept should **not** be used in combination with anakinra or TNF-blocking agents
Contraindications There are no contraindications listed within the manufacturer's U.S. labeling.

Canadian labeling: Hypersensitivity to abatacept or any component of the formulation; patients with, or at risk of sepsis syndrome (eg, immunocompromised, HIV positive)
Warnings/Precautions Serious and potentially fatal infections (including tuberculosis and sepsis) have been reported, particularly in patients receiving concomitant immunosuppressive therapy. RA patients receiving a concomitant TNF antagonist experienced an even higher rate of serious infection. Caution should be exercised when considering the use of abatacept in any patient with a history of recurrent infections, with conditions that predispose them to infections, or with chronic, latent, or localized infections. Patients who develop a new infection while undergoing treatment should be monitored closely. If a patient develops a serious infection, abatacept should be discontinued. Screen patients for latent tuberculosis infection prior to initiating abatacept; safety in tuberculosis-positive patients has not been established. Treat patients testing positive according to standard therapy prior to initiating abatacept. Adult patients receiving abatacept in combination with TNF-blocking agents had higher rates of infections (including serious infections) than patients on TNF-blocking agents alone. Potentially significant drug-drug interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. The manufacturer does not recommend concurrent use with anakinra or TNF-blocking agents. Monitor for signs and symptoms of infection when transitioning from TNF-blocking agents to abatacept. Due to the effect of T-cell inhibition on host defenses, abatacept may affect immune responses against infections and malignancies; impact on the development and course of malignancies is not fully defined.

Use caution with chronic obstructive pulmonary disease (COPD), higher incidences of adverse effects (COPD exacerbation, cough, rhonchi, dyspnea) have been observed; monitor closely. Rare cases of hypersensitivity, anaphylaxis, or anaphylactoid reactions have been reported with intravenous administration; may occur with first infusion. Some reactions (hypotension, urticaria, dyspnea) occurred within 24 hours of infusion. Discontinue treatment if anaphylaxis or other serious allergic reaction occurs; medications for the treatment of hypersensitivity reactions should be available for immediate use. Patients should be screened for viral hepatitis prior to use; antirheumatic therapy may cause reactivation of hepatitis B. Patients should be brought up to date with all immunizations before initiating therapy. Live vaccines should not be given concurrently or within 3 months of discontinuation of therapy; there is no data available concerning secondary transmission of live vaccines in patients receiving therapy. Powder for injection may contain maltose, which may result in falsely-elevated serum glucose readings on the day of infusion. Higher incidences of infection and malignancy were observed in the elderly; use with caution.
Adverse Reactions (Reflective of adult population; not specific for elderly) **Note:** Percentages not always reported; COPD patients experienced a higher frequency of COPD-related adverse reactions (COPD exacerbation, cough, dyspnea, pneumonia, rhonchi)

>10%:
Central nervous system: Headache (≤18%)
Gastrointestinal: Nausea
Respiratory: Nasopharyngitis (12%), upper respiratory tract infection
Miscellaneous: Infection (adults 54%; children 36%), antibody development (2% to 41%)
1% to 10%:
Cardiovascular: Hypertension (7%)
Central nervous system: Dizziness (9%)
Dermatologic: Skin rash (4%)
Gastrointestinal: Dyspepsia (6%), abdominal pain, diarrhea
Genitourinary: Urinary tract infection (6%)
Immunologic: Immunogenicity (1% to 2%)
Infection: Herpes simplex infection, influenza
Local: Injection site reaction (3%)
Neuromuscular & skeletal: Back pain (7%), limb pain (3%)
Respiratory: Cough (8%), bronchitis, pneumonia, rhinitis, sinusitis
Miscellaneous: Infusion-related reaction (≤9%), fever
Drug Interactions
Metabolism/Transport Effects None known.
Avoid Concomitant Use
Avoid concomitant use of Abatacept with any of the following: Anakinra; Anti-TNF Agents; BCG (Intravesical); Belimumab; Natalizumab; Pimecrolimus; RiTUXimab; Tacrolimus (Topical); Tocilizumab; Tofacitinib; Vaccines (Live)
Increased Effect/Toxicity
Abatacept may increase the levels/effects of: Belimumab; Leflunomide; Natalizumab; Tofacitinib; Vaccines (Live)

The levels/effects of Abatacept may be increased by: Anakinra; Anti-TNF Agents; Denosumab; Pimecrolimus; RiTUXimab; Roflumilast; Tacrolimus (Topical); Tocilizumab; Trastuzumab
Decreased Effect
Abatacept may decrease the levels/effects of: BCG (Intravesical); Coccidioides immitis Skin Test; Sipuleucel-T; Vaccines (Inactivated); Vaccines (Live)

The levels/effects of Abatacept may be decreased by: Echinacea
Preparation for Administration
IV: Reconstitute each vial with 10 mL SWFI using the provided silicone-free disposable syringe (discard solutions accidentally reconstituted with siliconized syringe as they may develop translucent particles). Inject SWFI down the side of the vial to avoid foaming. The reconstituted solution contains 25 mg/mL abatacept. Further dilute (using a silicone-free syringe) in 100 mL NS to a final concentration of ≤10 mg/mL. Prior to adding abatacept to the 100 mL bag, the manufacturer recommends withdrawing a volume of NS equal to the abatacept volume required, resulting in a final volume of 100 mL. Mix gently; do not shake.
SubQ: Allow prefilled syringe to reach room temperature prior to administration by removing from refrigerator 30-60 minutes prior to administration.
Storage/Stability
Prefilled syringe: Store at 2°C to 8°C (36°F to 46°F); do not freeze. Protect from light.

Powder for injection: Prior to reconstitution, store at 2°C to 8°C (36°F to 46°F); do not freeze. Protect from light. After dilution, may be stored for up to 24 hours at room temperature or refrigerated at 2°C to 8°C (36°F to 46°F). Must be used within 24 hours of reconstitution.

Mechanism of Action Selective costimulation modulator; inhibits T-cell (T-lymphocyte) activation by binding to CD80 and CD86 on antigen presenting cells (APC), thus blocking the required CD28 interaction between APCs and T cells. Activated T lymphocytes are found in the synovium of rheumatoid arthritis patients.

Pharmacodynamics/Kinetics

Bioavailability: SubQ: 78.6% (relative to IV administration)
Distribution: V_{ss}: 0.02-0.13 L/kg
Half-life elimination: 8-25 days

Dosage

Geriatric Refer to Dosage: Adult. Due to potential for higher rates of infections and malignancies, use caution.

Adult

Rheumatoid arthritis (RA):

IV: Dosing is according to body weight. Following the initial IV infusion (using the weight-based dosing), repeat IV infusion (using the same weight-based dosing) at 2 weeks and 4 weeks after the initial infusion, and every 4 weeks thereafter.
<60 kg: 500 mg
60-100 kg: 750 mg
>100 kg: 1000 mg

SubQ: 125 mg subcutaneously once weekly. **Note:** SubQ dosing may be initiated with or without an IV loading dose.

If initiating with an IV loading dose, administer the initial IV infusion (using the weight-based dosing), then administer 125 mg subcutaneously within 24 hours of the infusion, followed by 125 mg subcutaneously once weekly thereafter.

If transitioning from IV therapy to SubQ therapy, administer the first SubQ dose instead of the next scheduled IV dose.

Renal Impairment No dosage adjustment provided in manufacturer's labeling (has not been studied).

Hepatic Impairment No dosage adjustment provided in manufacturer's labeling (has not been studied).

Administration

IV: Infuse over 30 minutes. Administer through a 0.2-1.2 micron low protein-binding filter

SubQ: Allow prefilled syringe to warm to room temperature (for 30-60 minutes) prior to administration. Inject into the front of the thigh (preferred), abdomen (except for 2-inch area around the navel), or the outer area of the upper arms (if administered by a caregiver). Rotate injection sites (≥1 inch apart); do not administer into tender, bruised, red, or hard skin.

Monitoring Parameters Signs and symptoms of infection, signs and symptoms of hypersensitivity reaction; hepatitis and TB screening prior to therapy initiation

Test Interactions Contains maltose; may result in falsely elevated blood glucose levels with dehydrogenase pyrroloquinolinequinone or glucose-dye-oxidoreductase testing methods on the day of infusion. Glucose monitoring methods which utilize glucose dehydrogenase nicotine adenine dinucleotide (GDH-NAD), glucose oxidase, or glucose hexokinase are recommended.

Special Geriatric Considerations The number of elderly (≥65 years of age) were insufficient to draw significant clinical conclusions. The studies to date have not demonstrated any differences in safety and efficacy between young adults and elderly. However, the frequency of infections and malignancy was higher in those >65 years of age than those <65 years. Since elderly experience a higher incidence of infections and malignancies, use abatacept with caution in this population.

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution Prefilled Syringe, Subcutaneous [preservative free]:
Orencia: 125 mg/mL (1 mL)

Solution Reconstituted, Intravenous [preservative free]:
Orencia: 250 mg (1 ea)

- **Abbott-43818** *see* Leuprolide *on page 913*
- **ABCD** *see* Amphotericin B Cholesteryl Sulfate Complex *on page 94*
- **Abelcet** *see* Amphotericin B (Lipid Complex) *on page 98*
- **Abilify** *see* ARIPiprazole *on page 115*
- **Abilify Discmelt [DSC]** *see* ARIPiprazole *on page 115*
- **Abilify Maintena** *see* ARIPiprazole *on page 115*
- **Abiraterone** *see* Abiraterone Acetate *on page 19*

Abiraterone Acetate (a bir A ter one AS e tate)

Medication Safety Issues

Sound-alike/look-alike issues:
Zytiga may be confused with Jevtana, Xgeva, Xofigo, Xtandi, Zometa, Zydelig

Brand Names: US Zytiga

Brand Names: Canada Zytiga

Index Terms Abiraterone; CB7630

Generic Availability (US) No

Pharmacologic Category Antiandrogen; Antineoplastic Agent, Antiandrogen

Use Prostate cancer: Treatment of metastatic, castration-resistant prostate cancer (in combination with prednisone)

Contraindications

Canadian labeling: Additional contraindication (not in US labeling): Hypersensitivity to abiraterone acetate or any component of the formulation or container

Warnings/Precautions Hazardous agent - use appropriate precautions for handling and disposal (NIOSH 2014 [group 1]). Significant increases in liver enzymes have been reported (higher likelihood in patients with baseline elevations), generally occurring in the first 3 months of treatment. May require dosage reduction, treatment interruption, and/ or discontinuation. ALT, AST, and bilirubin should be monitored prior to treatment, every 2 weeks for 3 months and monthly thereafter; patients with hepatic impairment, elevations in liver function tests, or experiencing hepatotoxicity require more frequent monitoring (see Dosage: Hepatic Impairment and Monitoring Parameters). Evaluate liver function promptly with signs or symptoms of hepatotoxicity. The safety of retreatment after significant elevations (ALT or AST >20 times the upper limit of normal [ULN] and/or total bilirubin >10 times ULN) has not been evaluated. Do not use in patients with preexisting severe hepatic impairment (Child-Pugh class C); dosage reduction is recommended in patients with baseline moderate impairment. Canadian labeling (not in U.S. labeling) also recommends avoiding use in patients with preexisting moderate hepatic impairment.

Concurrent infection, stress, or interruption of daily corticosteroids is associated with reports of adrenocortical insufficiency. Monitor closely for signs and symptoms of adrenocorticoid insufficiency, which could be masked by adverse events associated with mineralocorticoid excess. Diagnostic testing for adrenal insufficiency may be clinically indicated. Increased corticosteroid doses may be required before, during, and after stress. May cause increased mineralocorticoid levels, which may result in hypertension, hypokalemia and fluid retention (including grades 3 and 4 events). Concomitant administration with corticosteroids reduces the incidence and severity of these