Abiraterone: Drug information

(For additional information see "Abiraterone: Patient drug information ")

For abbreviations and symbols that may be used in Lexicomp (show table)

Brand Names: US

Zytiga

Brand Names: Canada

Zytiga

Pharmacologic Category

Antiandrogen; Antineoplastic Agent, Antiandrogen

Dosing: Adult

Prostate cancer, metastatic, castration-resistant: Oral: 1,000 mg once daily (in combination with prednisone 5 mg twice daily)

Prostate cancer, metastatic or high-risk locally advanced, castration-sensitive (off-label use): Oral: 1,000 mg once daily (in combination with prednisone 5 mg once daily and androgen-deprivation therapy; Fizazi 2017) **or** 1,000 mg once daily (in combination with prednisolone 5 mg once daily and androgen-deprivation therapy; James 2017)

Dosage adjustment for concomitant strong CYP3A4 inducers: Avoid concomitant strong CYP3A4 inducers; if a strong CYP3A4 inducer must be administered concurrently, increase the abiraterone frequency to twice daily (eg, from 1,000 mg once daily to 1,000 mg twice daily). Upon discontinuation of the strong CYP3A4 inducer, reduce abiraterone back to the prior dose and frequency.

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

No dosage adjustment necessary.

Dosing: Hepatic Impairment

Hepatic impairment ***prior to*** treatment initiation:

Mild (Child-Pugh class A): No dosage adjustment necessary.

Moderate (Child-Pugh class B): 250 mg once daily. Permanently discontinue if ALT and/or AST >5 times the upper limit of normal (ULN) or total bilirubin >3 times ULN occur during treatment in patients with baseline moderate hepatic impairment.

Severe (Child-Pugh class C): Do not use.

Hepatotoxicity ***during*** treatment:

ALT and/or AST >5 times ULN **or** total bilirubin >3 times ULN: Withhold treatment until liver function tests return to baseline or ALT and AST ≤2.5 times ULN and total bilirubin ≤1.5 times ULN, then reinitiate at 750 mg once daily.

Recurrent hepatotoxicity on 750 mg/day: Withhold treatment until liver function tests return to baseline or ALT and AST ≤2.5 times ULN and total bilirubin ≤1.5 times ULN, then reinitiate at 500 mg once daily.

Recurrent hepatotoxicity on 500 mg once daily: Discontinue treatment

ALT >3 times ULN **and** total bilirubin >2 times ULN (in the absence of biliary obstruction or other contributing cause responsible for concurrent elevation): Permanently discontinue treatment

Dosing: Adjustment for Toxicity

Hepatotoxicity: Refer to Dosing: Hepatic Impairment.

Dosage Forms

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

Tablet, Oral:

Zytiga: 250 mg, 500 mg

Generic Equivalent Available (US)

No

Dosage Forms Considerations

Zytiga 250 mg tablets are produced in film-coated, and uncoated tablets; only the uncoated tablets are available in the United States. Zytiga 500 mg tablets are film-coated.

Dosage Forms: Canada

Information with regard to form, strength, and availability of products uniquely available in Canada but currently not available in the US. Refer also to Dosage forms.

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

Tablet, Oral:

Zytiga: 250mg, 500 mg [film-coated]

Administration

Administer abiraterone orally on an empty stomach, at least 1 hour before and 2 hours after food. **Note:** The prescribing information describes when to give food with respect to abiraterone; no food should be consumed for at least 2 hours before or for at least 1 hour after the abiraterone dose. Swallow tablets whole with water. Do not crush or chew.

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage. NIOSH recommends single gloving for administration of intact tablets or capsules (NIOSH 2016).

Use

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

Use: Off-Label

Prostate cancer, metastatic or high-risk locally advanced, castration-sensitive

Medication Safety Issues

Sound-alike/look-alike issues:

Zytiga may be confused with Jevtana, Xgeva, Xofigo, Xtandi, Zometa, Zydelig

Adverse Reactions

Adverse reactions reported for use in combination with prednisone.

>10%:

Cardiovascular: Edema (25% to 27%), hypertension (9% to 22%)

Central nervous system: Fatigue (39%), insomnia (14%)

Dermatologic: Bruise (13%)

Endocrine & metabolic: Hypertriglyceridemia (63%), hyperglycemia (57%), hypernatremia (33%), hypokalemia (17% to 28%), hypophosphatemia (24%), hot flash (19% to 22%)

Gastrointestinal: Constipation (23%), diarrhea (18% to 22%), dyspepsia (6% to 11%)

Genitourinary: Urinary tract infection (12%)

Hematologic & oncologic: Lymphocytopenia (38%; grades 3/4: 9%)

Hepatic: Increased serum ALT (11% to 42%), increased serum AST (37%)

Neuromuscular & skeletal: Joint swelling (30%), myalgia (26%)

Respiratory: Cough (11% to 17%), upper respiratory infection (5% to 13%), dyspnea (12%), nasopharyngitis (11%)

1% to 10%:

Cardiovascular: Cardiac arrhythmia (7%), chest pain (4%), cardiac failure (2%)

Central nervous system: Falling (6%)

Dermatologic: Skin rash (8%)

Genitourinary: Hematuria (10%), groin pain (7%), urinary frequency (7%), nocturia (6%)

Hepatic: Increased serum bilirubin (7%)

Neuromuscular & skeletal: Bone fracture (6%)

Miscellaneous: Fever (9%)

<1%, postmarketing, and/or case reports: Acute hepatic failure, adrenocortical insufficiency, fulminant hepatitis, myopathy, pneumonitis

Contraindications

Women who are or may become pregnant

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

Warnings/Precautions

Concerns related to adverse effects:

• Adrenocortical insufficiency: 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.

• Hepatotoxicity: Severe hepatotoxicity (eg, fulminant hepatitis, acute liver failure, and death) has been reported. Significant increases in liver enzymes have also been observed (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 adjustment for 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.

• Mineralocorticoid excess: Increased mineralocorticoids due to CYP17 inhibition may result in hypertension, hypokalemia, and fluid retention (including grade 3 and 4 events). Monitor at least monthly for hypertension, hypokalemia, and fluid retention. Concomitant administration with corticosteroids reduces the incidence and severity of these adverse events.

Disease-related concerns:

• Cardiovascular disease: May cause hypertension, hypokalemia, and fluid retention. Control hypertension and correct hypokalemia prior to and during treatment. Use with caution in patients with cardiovascular disease, particularly with heart failure, recent MI, or ventricular arrhythmia. Patients with left ventricular ejection fraction (LVEF) <50% or NYHA class II, III, or IV heart failure were excluded from clinical trials. Monitor at least monthly for hypertension, hypokalemia, and fluid retention.

• Hepatic impairment: Do not use in patients with preexisting severe hepatic impairment (Child-Pugh class C); dosage reduction is recommended in patients with baseline moderate impairment.

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Other warnings/precautions:

• Food: Abiraterone must be administered on an empty stomach (administer at least 1 hour before and 2 hours after any food); abiraterone AUC (exposure) may be increased up to 10-fold if administered with a meal.

Metabolism/Transport Effects

Substrate of CYP3A4 (major); **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential; **Inhibits** CYP2C8 (weak), CYP2C9 (moderate), CYP2D6 (moderate), OATP1B1/SLCO1B1

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Amodiaquine: CYP2C8 Inhibitors may increase the serum concentration of Amodiaquine. *Risk X: Avoid combination*

Bosentan: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers). *Risk C: Monitor therapy*

Bosentan: CYP2C9 Inhibitors (Moderate) may increase the serum concentration of Bosentan. Management: Concomitant use of both a CYP2C9 inhibitor and a CYP3A inhibitor or a single agent that inhibits both enzymes with bosentan is likely to cause a large increase in serum concentrations of bosentan and is not recommended. See monograph for details. *Risk C: Monitor therapy*

Cannabis: CYP2C9 Inhibitors (Moderate) may increase the serum concentration of Cannabis. More specifically, tetrahydrocannabinol serum concentrations may be increased. *Risk C: Monitor therapy*

Choline C 11: Antiandrogens may diminish the therapeutic effect of Choline C 11. *Risk C: Monitor therapy*

CloZAPine: CYP2D6 Inhibitors (Moderate) may increase the serum concentration of CloZAPine. *Risk C: Monitor therapy*

Codeine: CYP2D6 Inhibitors (Moderate) may diminish the therapeutic effect of Codeine. These CYP2D6 inhibitors may prevent the metabolic conversion of codeine to its active metabolite morphine. *Risk C: Monitor therapy*

CYP1A2 Substrates (High risk with Inhibitors): Abiraterone Acetate may increase the serum concentration of CYP1A2 Substrates (High risk with Inhibitors). *Risk C: Monitor therapy*

CYP2C8 Substrates (High risk with Inhibitors): Abiraterone Acetate may increase the serum concentration of CYP2C8 Substrates (High risk with Inhibitors). *Risk C: Monitor therapy*

CYP2C9 Substrates (High risk with Inhibitors): CYP2C9 Inhibitors (Moderate) may decrease the metabolism of CYP2C9 Substrates (High risk with Inhibitors). *Risk C: Monitor therapy*

CYP2D6 Substrates (High risk with Inhibitors): Abiraterone Acetate may increase the serum concentration of CYP2D6 Substrates (High risk with Inhibitors). Management: Avoid concurrent use of abiraterone with CYP2D6 substrates that have a narrow therapeutic index whenever possible. When concurrent use is not avoidable, monitor patients closely for signs/symptoms of toxicity. *Risk D: Consider therapy modification*

CYP3A4 Inducers (Moderate): May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers). *Risk C: Monitor therapy*

CYP3A4 Inducers (Strong): May decrease the serum concentration of Abiraterone Acetate. Management: Avoid whenever possible. If such a combination cannot be avoided, increase abiraterone acetate dosing frequency from once daily to twice daily during concomitant use. *Risk X: Avoid combination*

Dabrafenib: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers). Management: Seek alternatives to the CYP3A4 substrate when possible. If concomitant therapy cannot be avoided, monitor clinical effects of the substrate closely (particularly therapeutic effects). *Risk D: Consider therapy modification*

Deferasirox: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers). *Risk C: Monitor therapy*

DOXOrubicin (Conventional): CYP2D6 Inhibitors (Moderate) may increase the serum concentration of DOXOrubicin (Conventional). Management: Seek alternatives to moderate CYP2D6 inhibitors in patients treated with doxorubicin whenever possible. One U.S. manufacturer (Pfizer Inc.) recommends that these combinations be avoided. *Risk D: Consider therapy modification*

Dronabinol: CYP2C9 Inhibitors (Moderate) may increase the serum concentration of Dronabinol. *Risk C: Monitor therapy*

Eliglustat: CYP2D6 Inhibitors (Moderate) may increase the serum concentration of Eliglustat. Management: Reduce the eliglustat dose to 84 mg daily. Avoid use of eliglustat in combination with a moderate CYP2D6 inhibitor and a strong or moderate CYP3A4 inhibitor. *Risk D: Consider therapy modification*

Fesoterodine: CYP2D6 Inhibitors may increase serum concentrations of the active metabolite(s) of Fesoterodine. *Risk C: Monitor therapy*

Indium 111 Capromab Pendetide: Antiandrogens may diminish the diagnostic effect of Indium 111 Capromab Pendetide. *Risk X: Avoid combination*

Metoprolol: CYP2D6 Inhibitors may increase the serum concentration of Metoprolol. Management: Consider an alternative for one of the interacting drugs in order to avoid metoprolol toxicity. If the combination must be used, monitor response to metoprolol closely. Metoprolol dose reductions may be necessary. *Risk D: Consider therapy modification*

Nebivolol: CYP2D6 Inhibitors (Moderate) may increase the serum concentration of Nebivolol. *Risk C: Monitor therapy*

Perhexiline: CYP2D6 Inhibitors may increase the serum concentration of Perhexiline. Management: Consider alternatives to this combination if possible. If combined, monitor for increased perhexiline serum concentrations and toxicities (eg, hypoglycemia, neuropathy, liver dysfunction). Perhexiline dose reductions will likely be required. *Risk D: Consider therapy modification*

Pitolisant: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers). Management: Combined use of pitolisant with a CYP3A4 substrate that has a narrow therapeutic index should be avoided. Other CYP3A4 substrates should be monitored more closely when used with pitolisant. *Risk D: Consider therapy modification*

Sarilumab: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers). *Risk C: Monitor therapy*

Siltuximab: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers). *Risk C: Monitor therapy*

Spironolactone: May diminish the therapeutic effect of Abiraterone Acetate. *Risk C: Monitor therapy*

St John's Wort: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers). Management: Consider an alternative for one of the interacting drugs. Some combinations may be specifically contraindicated. Consult appropriate manufacturer labeling. *Risk D: Consider therapy modification*

Tamoxifen: CYP2D6 Inhibitors (Moderate) may decrease serum concentrations of the active metabolite(s) of Tamoxifen. Specifically, CYP2D6 inhibitors may decrease the metabolic formation of highly potent active metabolites. Management: Consider alternatives with less of an inhibitory effect on CYP2D6 activity when possible. *Risk D: Consider therapy modification*

Tetrahydrocannabinol: CYP2C9 Inhibitors (Moderate) may increase the serum concentration of Tetrahydrocannabinol. *Risk C: Monitor therapy*

Thioridazine: CYP2D6 Inhibitors may increase the serum concentration of Thioridazine. *Risk X: Avoid combination*

Tocilizumab: May decrease the serum concentration of CYP3A4 Substrates (High risk with Inducers). *Risk C: Monitor therapy*

TraMADol: CYP2D6 Inhibitors (Moderate) may diminish the therapeutic effect of TraMADol. These CYP2D6 inhibitors may prevent the metabolic conversion of tramadol to its active metabolite that accounts for much of its opioid-like effects. *Risk C: Monitor therapy*

Food Interactions

Taking abiraterone with food will increase systemic exposure (up to 10-fold). Management: Do not administer with food. Abiraterone must be taken on an empty stomach, at least 1 hour before and 2 hours after food.

Pregnancy Risk Factor

X (show table)

Pregnancy Implications

Based on the mechanism of action and adverse effects observed in animal reproduction studies, abiraterone may cause fetal harm or fetal loss if administered during pregnancy. Abiraterone is not indicated for use in women and is specifically contraindicated in women who are or may become pregnant. Abiraterone is available in uncoated and film-coated tablets; the manufacturer recommends women who are or may become pregnant wear gloves if handling uncoated tablets. NIOSH recommends single gloving for administration of hazardous intact oral tablets (NIOSH 2016).

It is not known if abiraterone is excreted in semen; therefore, men should use a condom and another method

of birth control during treatment and for 1 week following therapy if having intercourse with a woman of reproductive age.

Breast-Feeding Considerations It is not known if abiraterone is present in breast milk. Abiraterone is not indicated for use in women.

Monitoring Parameters ALT, AST, and bilirubin prior to treatment, every 2 weeks for 3 months and monthly thereafter; if baseline moderate hepatic impairment (Child-Pugh class B), monitor ALT, AST, and bilirubin prior to treatment, weekly for the first month, every 2 weeks for 2 months then monthly thereafter. If hepatotoxicity develops during treatment (and only after therapy is interrupted and liver function tests have returned to safe levels), monitor ALT, AST, and bilirubin every 2 weeks for 3 months and monthly thereafter. Monitoring of testosterone levels is not necessary. Serum potassium (prior to treatment and at least monthly).

Monitor for signs and symptoms of adrenocorticoid insufficiency; if clinically indicated, consider appropriate diagnostics to confirm adrenal insufficiency. Monitor blood pressure and for fluid retention (prior to treatment and at least monthly). Monitor adherence.

Mechanism of Action Selectively and irreversibly inhibits CYP17 (17 alpha-hydroxylase/C17,20-lyase), an enzyme required for androgen biosynthesis which is expressed in testicular, adrenal, and prostatic tumor tissues. Inhibits the formation of the testosterone precursors dehydroepiandrosterone (DHEA) and androstenedione.

Pharmacodynamics/Kinetics

Distribution: V_{dss}: 19,669 ± 13,358 L

Protein binding: >99%; to albumin and alpha$_1$-acid glycoprotein

Metabolism: Abiraterone acetate is hydrolyzed to the active metabolite abiraterone; further metabolized to inactive metabolites abiraterone sulphate and N-oxide abiraterone sulphate via CYP3A4 and SULT2A1

Bioavailability: Systemic exposure is increased by food

Half-life elimination: 14.4 to 16.5 hours (Acharya 2012); prolonged in patients with mild and moderate hepatic impairment, ~18 and ~19 hours, respectively

Time to peak: 2 hours (Acharya 2012)

Excretion: Feces (~88%); urine (~5%)

Pricing: US

Tablets (Zytiga Oral)

250 mg (120): $11275.06

500 mg (60): $11275.06

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes

only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

Brand Names: International Abiron (LK); Aizerone (LK); Xbira (IN); Zytiga (AE, AR, AU, BE, BR, BZ, CH, CL, CN, CO, CR, CY, CZ, DE, DK, DO, EC, EE, ES, FR, GB, GT, HK, HN, HR, HU, ID, IE, IL, IS, JO, JP, KR, KW, LB, LK, LT, LU, LV, MT, MX, MY, NI, NL, NO, NZ, PA, PH, PL, PT, QA, RO, SA, SE, SG, SI, SK, SV, TH, TR, VN); Zytix (BD); Zytyha (UA); Zyvalyx (EC)

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