Yonsa®
(abiraterone acetate)
125 mg tablets

TRICARE® AND YONSA®

TRICARE has designated YONSA® as the Department of Defense's Preferred CYP-17 Inhibitor agent on the Uniform/TRICARE Formulary.[1] All new patients and current users of ZYTIGA® (abiraterone acetate)/generics are required to try YONSA® first, unless they have already tried YONSA®, or they have or have had a contraindication, inadequate response, or adverse reaction to YONSA® that is not expected to occur with the requested agent.[1]

YONSA®, in combination with methylprednisolone, is the first and only micronized formulation of abiraterone acetate for the treatment of metastatic castration-resistant prostate cancer (mCRPC) with a Tier 1 co-pay.[2]

Proprietary YONSA® Micronization Provides:

RAPID ABSORPTION
Increases surface area for rapid dissolution and absorption.[3]

LOW 500 MG DOSE
Four 125 mg tablets, plus 4 mg methylprednisolon.[2,3]

FLEXIBLE DOSING
Patients can take YONSA® with or without food.[2,4]

The TRICARE and Sun Pharmaceuticals partnership offers the military another option for mCRPC therapy.

Pills not of actual size.

INDICATION

YONSA® (abiraterone acetate) in combination with methylprednisolone is indicated for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypertension, Hypokalemia, and Fluid Retention Due to Mineralocorticoid Excess: YONSA® may cause hypertension, hypokalemia, and fluid retention due to increased mineralocorticoid levels resulting from CYP17 inhibition. Monitor patients at least once a month. Control hypertension and correct hypokalemia before and during treatment with YONSA®.

Closely monitor patients whose underlying medical conditions might be compromised by increases in blood pressure, hypokalemia, or fluid retention, such as those with heart failure, recent myocardial infarction, cardiovascular disease, or ventricular arrhythmia. In postmarketing experience, QT prolongation and Torsades de Pointes have been observed in patients who develop hypokalemia while taking abiraterone acetate.

The safety of YONSA® in patients with left ventricular ejection fraction <50%, or New York Heart Association (NYHA) Class III or IV heart failure (in Study 1) or NYHA Class II to IV heart failure (in Study 2), was not evaluated because these patients were excluded from randomized clinical trials.

Adrenocortical Insufficiency: Adrenocortical insufficiency (AI) was reported in patients receiving abiraterone acetate in combination with corticosteroid, following an interruption of daily steroids and/or with concurrent infection or stress. Monitor patients for symptoms and signs of AI, particularly if patients are withdrawn from corticosteroids, have corticosteroid dose reductions, or experience unusual stress. Symptoms and signs of AI may be masked by adverse reactions associated with mineralocorticoid excess seen in patients treated with YONSA®. Perform appropriate tests, if indicated, to confirm AI. Increased dosages of corticosteroids may be used before, during, and after stressful situations.

Please see additional Important Safety Information on reverse side and accompanying Full Prescribing Information.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

Hepatotoxicity: In postmarketing experience, there has been abiraterone acetate-associated severe hepatic toxicity, including reports of fulminant hepatitis, acute liver failure, and deaths. Measure serum transaminases (ALT and AST) and bilirubin levels prior to starting treatment with YONSA®, every two weeks for the first three months of treatment, and monthly thereafter. In patients with baseline moderate hepatic impairment receiving a reduced YONSA® dose of 125 mg, measure ALT, AST, and bilirubin prior to the start of treatment, every week for the first month, every two weeks for the following two months of treatment, and monthly thereafter.

Promptly measure serum total bilirubin, AST, and ALT if clinical symptoms or signs suggestive of hepatotoxicity develop. Elevations of AST, ALT, or bilirubin from the patient's baseline should prompt more frequent monitoring. If at any time AST or ALT rise above five times the upper limit of normal (ULN), or the bilirubin rises above three times the ULN, interrupt YONSA® treatment and closely monitor liver function.

Re-treatment with YONSA® at a reduced dose level may take place only after return of liver function tests to the patient's baseline, or to AST and ALT less than or equal to 2.5X ULN and total bilirubin less than or equal to 1.5X ULN.

Permanently discontinue treatment with abiraterone acetate for patients who develop a concurrent elevation of ALT greater than 3X ULN and total bilirubin greater than 2X ULN in the absence of biliary obstruction or other causes responsible for the concurrent elevation.

The safety of YONSA® re-treatment of patients who develop AST or ALT greater than or equal to 20X ULN and/or bilirubin greater than or equal to 10X ULN has not been evaluated.

Increased Fractures and Mortality in Combination with Radium Ra 223 Dichloride: YONSA® plus methylprednisolone is not recommended for use in combination with radium Ra 223 dichloride outside of clinical trials.

Increased incidences of fractures (28.6% vs 11.4%) and deaths (38.5% vs 35.5%) have been observed in patients who received abiraterone acetate plus a corticosteroid in combination with radium Ra 223 dichloride compared to patients who received placebo in combination with abiraterone acetate plus a corticosteroid.

Embryo-Fetal Toxicity: The safety and efficacy of YONSA® have not been established in females. Based on animal reproductive studies and mechanism of action, YONSA® can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment with YONSA® and for 3 weeks after the final dose of YONSA®.

Females who are pregnant or may be pregnant should not handle YONSA® tablets if broken, crushed, or damaged without protection, eg, gloves.

Hypoglycemia: Severe hypoglycemia has been reported when abiraterone acetate was administered to patients with pre-existing diabetes receiving medications containing thiazolidinediones (including pioglitazone) or repaglinide. Monitor blood glucose in patients with diabetes during and after discontinuation of treatment with abiraterone acetate. Assess if antidiabetic drug dosage needs to be adjusted to minimize the risk of hypoglycemia.

ADVERSE REACTIONS

The most common adverse reactions (≥10%) are fatigue, joint swelling or discomfort, edema, hot flush, diarrhea, vomiting, cough, hypertension, dyspnea, urinary tract infection, and contusion.

The most common laboratory abnormalities (>20%) are anemia, elevated alkaline phosphatase, hypertriglyceridemia, lymphopenia, hypercholesterolemia, hyperglycemia, elevated AST, hypophosphatemia, elevated ALT, and hypokalemia.

DRUG INTERACTIONS

Drugs that Inhibit or Induce CYP3A4 Enzymes: Based on *in vitro* data, YONSA® is a substrate of CYP3A4. In a drug interaction trial, co-administration of rifampin, a strong CYP3A4 inducer, decreased exposure of abiraterone by 55%. Avoid concomitant strong CYP3A4 inducers during YONSA® treatment. If a strong CYP3A4 inducer must be co-administered, increase the YONSA® dosing frequency only during the co-administration period.

Effects of Abiraterone on Drug-Metabolizing Enzymes: Abiraterone is an inhibitor of the hepatic drug-metabolizing enzymes CYP2D6 and CYP2C8. Avoid co-administration of abiraterone acetate with substrates of CYP2D6 with a narrow therapeutic index (eg, thioridazine). If alternative treatments cannot be used, exercise caution and consider a dose reduction of the concomitant CYP2D6 substrate drug. In a CYP2C8 drug-drug interaction trial in healthy subjects, the AUC of pioglitazone (CYP2C8 substrate) was increased by 46% when pioglitazone was given together with an abiraterone acetate single-dose equivalent to YONSA® 500 mg. Therefore, patients should be monitored closely for signs of toxicity related to a CYP2C8 substrate with a narrow therapeutic index if used concomitantly with abiraterone acetate.

Please see accompanying Full Prescribing Information.

References: 1. The official website of the Military Health System. DoD Pharmacy & Therapeutic Committee. https://health.mil/About-MHS/ OASDHA/Defense-Health-Agency/Operations/Pharmacy-Division/DoD-Pharmacy-and-Therapeutics-Committee. February 2019. Accessed July 2, 2019. **2.** YONSA® [prescribing information]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc; May 2018. **3.** Goldwater R, Hussaini A, Bosch B, Nemeth P. Comparison of a novel formulation of abiraterone acetate vs. the originator formulation in healthy male subjects: two randomized, open-label, crossover studies. *Clin Pharmacokinet.* 2017;56:803–813. **4.** Hussaini A, Olszanski AJ, Stein CA, Bosch B, Nemeth P. Impact of an alternative steroid on the relative bioavailability and bioequivalence of a novel versus the originator formulation of abiraterone acetate. *Cancer Chemo Pharmacol.* 2017;80(3):479–486.

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May 2021 PM-US-YON-0540