**ZYTIGA®** (abiraterone acetate) in combination with prednisone is indicated for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC).

**DRUG INTERACTIONS CAN BE AN IMPORTANT CONSIDERATION FOR PATIENTS WITH mCRPC.**

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**IMPORTANT SAFETY INFORMATION**

**Contraindications**—ZYTIGA® (abiraterone acetate) is not indicated for use in women. ZYTIGA® can cause fetal harm (Pregnancy Category X) when administered to a pregnant woman and is contraindicated in women who are or may become pregnant.

**Hypertension, Hypokalemia, and Fluid Retention Due to Mineralocorticoid Excess**—Use with caution in patients with a history of cardiovascular disease or with medical conditions that might be compromised by increases in blood pressure, hypokalemia, or fluid retention. ZYTIGA® may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition. Safety has not been established in patients with LVEF <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) because these patients were excluded from these randomized clinical trials. Control hypertension and correct hypokalemia before and during treatment. Monitor blood pressure, serum potassium, and symptoms of fluid retention at least monthly.

Please see reverse side for additional Important Safety Information and enclosed full Prescribing Information.

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### Drug Interactions for ZYTIGA®

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Considerations for ZYTIGA®</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZYTIGA® is a substrate of CYP3A4 based on in vitro data</td>
<td>Avoid concomitant strong CYP3A4 inducers during ZYTIGA® treatment. If a strong CYP3A4 inducer must be co-administered, increase the ZYTIGA® dosing frequency to twice a day only during the co-administration period (eg, from 1,000 mg once daily to 1,000 mg twice a day). Reduce the dose back to the previous dose and frequency if the concomitant strong CYP3A4 inducer is discontinued [see Dosage and Administration (2.3), Drug Interactions (7.1) and Clinical Pharmacology (12.3)].</td>
<td>phenytoin, carbamazepine, rifampin, rifabutin, rifapentine, phenobarbital¹</td>
</tr>
<tr>
<td>ZYTIGA® is an inhibitor of the hepatic drug-metabolizing enzyme CYP2D6</td>
<td>Avoid co-administration with CYP2D6 substrates with a narrow therapeutic index. If alternative treatments cannot be used, exercise caution and consider a dose reduction of the CYP2D6 substrate drug [see Drug Interactions (7.2) and Clinical Pharmacology (12.3)].</td>
<td>thioridazine¹</td>
</tr>
<tr>
<td>ZYTIGA® is an inhibitor of the hepatic drug-metabolizing enzyme CYP2C8</td>
<td>Patients should be monitored closely for signs of toxicity related to a CYP2C8 substrate with a narrow therapeutic index if used concomitantly with ZYTIGA® [see Drug Interactions (7.2) and Clinical Pharmacology (12.3)].</td>
<td>pioglitazone¹</td>
</tr>
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*In vitro* studies with human hepatic microsomes showed that abiraterone has the potential to inhibit CYP1A2, CYP2D6, CYP2C8, and to a lesser extent CYP2C9, CYP2C19 and CYP3A4/5.

*In vitro*, abiraterone and its major metabolites were shown to inhibit the hepatic uptake transporter OATP1B1. There are no clinical data available to confirm transporter-based interaction.
Adrenocortical Insufficiency (AI)—AI was reported in patients receiving ZYTIGA® (abiraterone acetate) in combination with prednisone, after an interruption of daily steroids and/or with concurrent infection or stress. Use caution and monitor for symptoms and signs of AI if prednisone is stopped or withdrawn, if prednisone dose is reduced, or if the patient experiences unusual stress. Symptoms and signs of AI may be masked by adverse reactions associated with mineralocorticoid excess seen in patients treated with ZYTIGA®. Perform appropriate tests, if indicated, to confirm AI. Increased dosages of corticosteroids may be used before, during, and after stressful situations.

Hepatotoxicity—In postmarketing experience, there have been ZYTIGA®-associated severe hepatic toxicities, including fulminant hepatitis, acute liver failure and deaths. Monitor liver function and modify, withhold, or discontinue ZYTIGA® dosing as recommended (see Prescribing Information for more information). Measure serum transaminases [alanine aminotransferase (ALT) and aspartate aminotransferase (AST)] and bilirubin levels prior to starting treatment with ZYTIGA®, every two weeks for the first three 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 ZYTIGA® treatment and closely monitor liver function. Re-treatment with ZYTIGA® 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 ZYTIGA® 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.

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—Based on in vitro data, ZYTIGA® 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 ZYTIGA® treatment. If a strong CYP3A4 inducer must be co-administered, increase the ZYTIGA® dosing frequency only during the co-administration period [see Dosage and Administration (2.3)]. In a dedicated drug interaction trial, co-administration of ketoconazole, a strong inhibitor of CYP3A4, had no clinically meaningful effect on the pharmacokinetics of abiraterone.

ZYTIGA® is an inhibitor of the hepatic drug-metabolizing enzymes CYP2D6 and CYP2C8. Avoid co-administration with CYP2D6 substrates with a narrow therapeutic index. If alternative treatments cannot be used, exercise caution and consider a dose reduction of the CYP2D6 substrate drug. In a CYP2C8 drug interaction trial in healthy subjects, the AUC of pioglitazone, a CYP2C8 substrate, was increased by 46% when administered with a single dose of ZYTIGA®. Patients should be monitored closely for signs of toxicity related to a CYP2C8 substrate with a narrow therapeutic index if used concomitantly with ZYTIGA®.

Use in Specific Populations—Do not use ZYTIGA® in patients with baseline severe hepatic impairment (Child-Pugh Class C).