

## ZYTIGA® (abiraterone acetate) ZYTIGA - Drug Interactions

### SUMMARY

- Following oral administration, abiraterone acetate is hydrolyzed to the active metabolite, abiraterone, likely through esterase activity.<sup>1</sup>
- Based on in vitro data, abiraterone is a substrate of CYP3A4. Strong inducers of CYP3A4 (eg, phenytoin, carbamazepine, rifampicin, rifabutin, rifapentine, phenobarbital) during treatment with ZYTIGA are to be avoided, or used with careful evaluation of clinical efficacy.<sup>2,3</sup> Please refer to the product labeling for additional information.
- Abiraterone acetate is an inhibitor of CYP2D6 and CYP2C8. Avoid coadministration of ZYTIGA with substrates of CYP2D6 with a narrow therapeutic index. If alternative treatments cannot be used, exercise caution and consider a dose reduction of the concomitant CYP2D6 substrate drug.<sup>4</sup> Clinicians should consider the therapeutic index of CYP2C8 substrate drugs when used concomitantly with ZYTIGA.<sup>5</sup>
- Additional relevant citations identified in the published literature are cited here.<sup>6,7</sup>

### DRUG INTERACTIONS

For up-to-date drug interaction, pharmacokinetic, and pharmacodynamic clinical data pertaining to specific medicinal agents, please review the local labeling of ZYTIGA and/or contact the manufacturers of these agents for additional information.

### LITERATURE SEARCH

A literature search of MEDLINE®, Embase®, BIOSIS Previews®, and Derwent Drug File (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 28 August 2024.

### REFERENCES

1. Acharya M, Gonzalez M, Mannens G, et al. A phase I, open-label, single-dose, mass balance study of 14C-labeled abiraterone acetate in healthy male subjects. *Xenobiotica*. 2013;43(4):379-389.
2. Bernard A, Vaccaro N, Acharya M, et al. Impact on abiraterone pharmacokinetics and safety: open-label drug-drug interaction studies with ketoconazole and rifampicin. *Clin Pharmacol Drug Dev*. 2015;4(1):63-73.
3. Data on File. Abiraterone Acetate CCDS v020. Janssen Research and Development, LLC. EDMS-ERI-22171594; 2021.
4. Center for drug evaluation and research. Clinical review of NDA 202379 - Zytiga™ (abiraterone acetate) for metastatic castration-resistant prostate cancer after prior chemotherapy. Center for drug evaluation and research; 2011. Accessed August 28, 2024.
5. Monbaliu J, Gonzalez M, Bernard A, et al. In vitro and in vivo drug-drug interaction studies to assess the effect of abiraterone acetate, abiraterone, and metabolites of abiraterone on CYP2C8 activity. *Drug Metab Dispos*. 2016;44(10):1682-1691.
6. Zhong YY, Anton A, Xie O, et al. Impact of comorbidities and drug interactions in patients with metastatic castration-resistant prostate cancer receiving androgen receptor pathway inhibitors. *JCO Oncol Pract*. 2024;00:1-12.
7. Armstrong AJ, Clarke N, Oya M, et al. Olaparib plus abiraterone for metastatic castration-resistant prostate cancer: pharmacokinetics data from the PROpel trial. *Eur Urol Oncol*. 2024;7(2):292-296.