RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Zytiga is indicated in combination with prednisone to treat men with late-stage (metastatic) castration-resistant prostate cancer, or prostate cancer that has spread to other parts of the body and is also resistant to medical or surgical treatments that lower testosterone. Zytiga is also indicated in combination with prednisone to treat men with metastatic high risk castration-sensitive prostate cancer. Zytiga targets a protein called cytochrome P450 17A1 (CYP17A1) which helps to prevent the conversion of androgens to testosterone and reduces the potential growth of prostate cancer cells (1).

Regulatory Status
FDA-approved indication: Zytiga is a CYP17 inhibitor indicated in combination with prednisone for the treatment of patients with: (1)

- Metastatic castration-resistant prostate cancer (CRPC)
- Metastatic high-risk castration-sensitive prostate cancer (CSPC)

Zytiga may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition. Zytiga should be used with caution in patients with a history of cardiovascular disease. Before treatment is initiated, hypertension should be controlled and hypokalemia corrected. Blood pressure, serum potassium, and symptoms of fluid retention should be monitored at least monthly. Adrenal cortical insufficiency may occur with the use of Zytiga. Adrenal insufficiency has occurred during Zytiga treatment. Caution should be used and monitor for symptoms and signs of adrenocortical insufficiency, particularly if patients are withdrawn from prednisone, have prednisone dose reductions, or experience unusual stress (1).

Zytiga may cause hepatotoxicity. Increases in liver enzymes have led to drug interruption, dose modification and/or discontinuation. Serum transaminases (ALT and AST) and bilirubin levels should be measured prior to initiation of therapy, every two weeks for the first three months of treatment, and monthly thereafter. 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, Zytiga treatment should be interrupted and liver function closely monitored (1).

Zytiga carries a pregnancy category X warning and is not indicated for use in women. Maternal use of an androgen receptor inhibitor could affect development of the fetus. If the patient has a partner who is pregnant or plans to become pregnant, a condom and another form of birth control must be used during and for 3 months after treatment (1).

The safety and effectiveness of Zytiga have not been established in pediatric patients (1).

**Summary**

Zytiga is a CYP17 inhibitor indicated for use in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer as well as for the treatment of metastatic high risk castration-sensitive prostate cancer. Zytiga may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition. Zytiga may cause adrenal insufficiency and hepatotoxicity. Zytiga carries a pregnancy category X warning and is not indicated for use in women. The safety and effectiveness of Zytiga have not been established in pediatric patients (1).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Zytiga while maintaining optimal therapeutic outcomes.

**References**