BlueCross BlueShield Federal Employee Program

JYNARQUE (tolvaptan)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Jynarque (tolvaptan) is a selective vasopressin V_{2-} receptor antagonist indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD). Decreasing binding of vasopressin to the V2-receptor in the kidney lowers adenylate cyclase activity resulting in a decrease in intracellular adenosine 3', 5-cyclic monophosphate (cAMP) concentrations. In clinical trials, decreased cAMP concentrations were associated with decreases in the rate of growth of total kidney volume and the rate of formation and enlargement of kidney cysts (1).

Regulatory Status

FDA approved indication: Jynarque is indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney disease (ADPKD) (1).

Jynarque is contraindicated if the patient has a history of signs or symptoms of significant liver impairment or injury, uncorrected abnormal blood sodium concentrations, unable to sense or respond to thirst, hypovolemia, hypersensitivity to tolvaptan or any of its components, uncorrected urinary outflow obstruction, or anuria (1).

Jynarque is contraindicated in patients with concomitant use of strong CYP3A inhibitors (such as ketoconazole, itraconazole, lopinavir/ritonavir, indinavir/ritonavir, ritonavir, and conivaptan).

To mitigate the risk of significant or irreversible liver injury, blood testing should be performed for ALT, AST, and bilirubin prior to initiation of Jynarque, at 2 and 4 weeks after initiation, monthly for 18 months and every 3 months thereafter. Monitor for concurrent symptoms that may indicate liver injury (1).

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

Summary

Jynarque (tolvaptan) is a selective vasopressin V_{2-} receptor antagonist indicated to slow kidney function decline in adults at risk of rapidly progressing autosomal dominant polycystic kidney

disease (ADPKD). Decreasing binding of vasopressin to the V2-receptor in the kidney lowers adenylate cyclase activity resulting in a decrease in intracellular adenosine 3', 5-cyclic monophosphate (cAMP) concentrations. In clinical trials, decreased cAMP concentrations were associated with decreases in the rate of growth of total kidney volume and the rate of formation and enlargement of kidney cysts Jynarque is contraindicated if the patient has a history of signs or symptoms of significant liver impairment or injury, concomitant use of strong CYP3A inhibitors (ketoconazole, itraconazole, lopinavir/ritonavir, indinavir/ritonavir, ritonavir, and conivaptan), uncorrected abnormal blood sodium concentrations, unable to sense or respond to thirst, hypovolemia, hypersensitivity to tolvaptan or any of its components, uncorrected urinary outflow obstruction, or anuria. Jynarque is available only through a restricted distribution program under a Risk Evaluation and Mitigation Strategy (REMS) because of the risks of liver injury (1).

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

References

1. Jynarque [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; October 2020.