YONDELIS (trabectedin)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Yondelis is an alkylating drug used for two types of unresectable or metastatic soft tissue sarcomas - liposarcoma or leiomyosarcoma. In soft tissue sarcomas, cancer cells form in the soft tissues of the body, including the muscles, tendons, fat, blood vessels, lymph vessels, nerves and tissues around joints. Liposarcoma and leiomyosarcoma are specific types of soft tissue sarcoma that occur in fat cells (liposarcoma) or smooth muscle cells (leiomyosarcoma). Soft tissue sarcomas can form almost anywhere in the body, but are most common in the head, neck, arms, legs, trunk and abdomen. Yondelis impairs DNA function resulting in a change of the cell cycle and eventual cell death (1).

Regulatory Status
FDA-approved indication: Yondelis is an alkylating drug indicated for the treatment of patients with unresectable or metastatic liposarcoma or leiomyosarcoma who received a prior anthracycline-containing regimen (1).

Dexamethasone should be administered intravenously 30 minutes prior to each dose of Yondelis to prevent hepatotoxicity and bone marrow toxicity (1).

Yondelis is associated with risk of neutropenic sepsis that can be fatal. Assess neutrophil count prior to administration of each dose of Yondelis and periodically throughout the treatment cycle (1). Yondelis can cause rhabdomyolysis and musculoskeletal toxicity that can be fatal. Assess CPK levels prior to each administration of Yondelis (1).

Hepatotoxicity, including hepatic failure, can occur with Yondelis. Use of Yondelis in patients with serum bilirubin levels above the upper limit of normal or with AST or ALT greater than 2.5 times the upper limit of normal has not been studied. Assess hepatic function prior to each administration of Yondelis (1).

Cardiomyopathy including cardiac failure, congestive heart failure, ejection fraction decreased, diastolic dysfunction, or right ventricular dysfunction can occur with Yondelis. In Trial 1, patients with a history of New York Heart Association Class II to IV heart failure or abnormal left ventricular ejection fraction (LVEF) at baseline were ineligible (1). LVEF was quantified as grade 1 (normal;
Yondelis is an alkylating drug indicated for the treatment of patients with unresectable or metastatic liposarcoma or leiomyosarcoma who received a prior anthracycline-containing regimen. Yondelis impairs DNA function resulting in a change of the cell cycle and eventual cell death. Patients prescribed Yondelis must have monitored platelets, neutrophil count, left ventricular ejection fraction, and hepatic function prior to each administration of Yondelis. Safety and effectiveness of Yondelis in patients less than 18 years of age have not been established (1).

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

References