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5.21.065

Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	December 4, 2015
Subject:	Yondelis	**Page:**	1 of 5

Last Review Date: March 8, 2024

Yondelis

Description

Yondelis (trabectedin)

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 rhabodmyolysis 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; ejection fraction [EF] 50% or greater), grade 2 (mild dysfunction; EF 40% to 49%), grade 3 (moderate dysfunction; EF 30% to 39%), grade 4 (severe dysfunction; EF 20% to 29%) or grade 5 (very severe dysfunction; EF 20% or less) (2). Assess left ventricular ejection fraction by echocardiogram or multigated acquisition scan before initiation of Yondelis and at 2- to 3-month intervals thereafter until Yondelis is discontinued (1).

Safety and effectiveness of Yondelis in patients less than 18 years of age have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Yondelis may be considered **medically necessary** if the conditions indicated below are met.

Yondelis may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Unresectable or metastatic liposarcoma
2. Unresectable or metastatic leiomyosarcoma

AND ALL of the following:

1. Prior therapy with anthracycline-containing chemotherapy regimen
2. Neutrophil count greater than 1500 cells/mL and monitor neutrophil count before each dose
3. Left ventricular ejection fraction (LVEF) is above 50%
4. AST or ALT levels < 2.5 x ULN prior to the start of therapy
5. Physician agrees to monitor hepatic function (LFTs) prior to each dose

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Unresectable or metastatic liposarcoma
2. Unresectable or metastatic leiomyosarcoma

AND ALL of the following:

1. **NO** disease progression or unacceptable toxicity
2. Neutrophil count greater than 1500 cells/mL and monitor neutrophil count before each dose
3. Physician agrees to monitor hepatic function (LFTs) prior to each dose
4. Left ventricular ejection fraction (LVEF) is above 50%

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

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

1. Yondelis [package insert]. Horsham, PA: Janssen Products; June 2020.
2. Zipes DP, Camm AJ, Borggrefe M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: J Am Coll Cardiol. 2006;48:e247–e346.
3. NCCN Drugs & Biologics Compendium® Trabectedin 2024. National Comprehensive Cancer Network, Inc. Accessed on January 12, 2024.

Policy History

Date	Action
December 2016	Addition to PA
March 2016	Annual editorial review Policy number change from 5.04.65 to 5.21.65
June 2016	Annual editorial review Change of the assessment of left ventricular ejection fraction (LVEF) by echocardiogram or multigated acquisition (MUGA) scan before initiation and every 3 months to left ventricular ejection fraction (LVEF) is above 50% per SME
September 2016	Annual review

June 2017	Annual editorial review and reference update Added age limit to renewal section
June 2018	Annual review and reference update
June 2019	Annual review and reference update
June 2020	Annual review
December 2021	Annual review and reference update
December 2022	Annual review and reference update. Changed policy number to 5.21.065
September 2023	Annual review and reference update
March 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.