Yondelis

(trabectedin)

New Product
Slideshow

MPR

Introduction

- **Brand name:** Yondelis
- **Generic name:** Trabectedin
- **Pharmacological class:** Alkylating agent
- **Strength and Formulation:** 1mg; per vial; lyophilized powder for IV infusion after reconstitution and dilution; contains sucrose
- **Manufacturer:** Janssen
- **How supplied:** Single-dose vial—1
- **Legal Classification:** Rx

YONDELIS


NDC 59676-610-01
Yondelis
(trabectedin)
for Injection
1 mg per vial
For Intravenous Infusion Only
Single dose
Discard any unused portion
Rx Only

Indications

- Treatment of unresectable or metastatic **liposarcoma** or **leiomyosarcoma** in patients who have received prior anthracycline-containing regimen

Dosage & Administration

- Give by IV infusion over 24 hours
- 1.5mg/m² every 21 days until disease progression or unacceptable toxicity
- **Moderate hepatic impairment:** 0.9mg/m² every 21 days
- **Premedicate** 30 minutes prior to each dose with IV dexamethasone 20mg
- Delay, reduce, or permanently discontinue dose according to severity of adverse reactions: see full labeling
- Do not increase dose in subsequent cycles once reduced

Considerations for Special Populations

- **Pregnancy:** Embryo-fetal toxicity; use effective contraception during and for 2 months (females) or 5 months (males) after final dose
- **Nursing mothers:** Not recommended
- **Pediatric:** <18 years: not established
- **Elderly:** Insufficient number of subjects studied
- **Hepatic impairment:** Severe impairment: not recommended

Warnings/Precautions

- Assess **neutrophil count** prior to each dose and periodically during the cycle; withhold if <1,500 cells/μL on day of dosing; permanently reduce dose if life-threatening or prolonged, severe neutropenia occurs in prior cycle

- Assess **CPK levels** prior to each dose; withhold if serum CPK >2.5XULN; permanently discontinue if rhabdomyolysis occurs

Warnings/Precautions

- Assess **LFTs** prior to each dose and as indicated based on pre-existing hepatic impairment; interrupt, reduce, or permanently discontinue dose based on severity/duration
- Assess **LVEF** by echocardiogram or MUGA scan prior to initiation and every 2–3 months thereafter until discontinued; withhold if LVEF below LLN; permanently discontinue if symptomatic cardiomyopathy occurs or persistent LV dysfunction not recover to LLN within 3 weeks

Interactions

- **Avoid** concomitant strong CYP3A inhibitors (eg, oral ketoconazole, itraconazole, posaconazole, voriconazole, clarithromycin, telithromycin, indinavir, lopinavir, ritonavir, boceprevir, nelfinavir, saquinavir, telaprevir, nefazodone, conivaptan), grapefruit or grapefruit juice
  - If short-term use (<14 days) necessary, give inhibitor 1 week after infusion and discontinue the day prior to next infusion
- **Avoid** concomitant strong CYP3A inducers (eg, rifampin, phenobarbital, St. John's wort)

Adverse Reactions

- Nausea
- Fatigue
- Vomiting
- Constipation
- Decreased appetite
- Diarrhea
- Peripheral edema
- Dyspnea
- Headache
- Neutropenia
- Thrombocytopenia
- Anemia
- Increased AST, CPK, ALT
- Anaphylaxis
- Neutropenic sepsis
- Rhabdomyolysis
- Hepatotoxicity
- Cardiomyopathy
- Extravasation
- Infertility

Mechanism of Action

- Trabectedin binds guanine residues in the minor groove of DNA, forming adducts and resulting in a bending of the DNA helix

- Adduct formation triggers a cascade of events that can affect the subsequent activity of DNA binding proteins, including some transcription factors, and DNA repair pathways, resulting in perturbation of the cell cycle and eventual cell death

Clinical Trials

- The safety and efficacy of Yondelis was evaluated in **Trial 1** (N=518), a randomized, open-label, active-controlled study that compared Yondelis vs. dacarbazine once every 3 weeks until disease progression or unacceptable toxicity in patients with metastatic or recurrent leiomyosarcoma or liposarcoma

Clinical Trials

- **Efficacy outcome measures** were progression-free survival (PFS), overall survival (OS), objective response rate (ORR), and duration of response

Clinical Trials

- Trial 1 showed a statistically significant improvement in **PFS**: 4.2 months in the Yondelis arm vs. 1.5 months in the dacarbazine arm (HR 0.55, 95% CI: 0.44, 0.70; $P<0.001$)

- **OS** was 13.7 months in the Yondelis arm vs. 13.1 months in the dacarbazine arm (HR 0.93, 95% CI: 0.75, 1.15; $P<0.49$)

Clinical Trials

- **ORR** was seen in 7% of patients in the Yondelis arm vs. 6% in the dacarbazine arm

- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

  http://www.empr.com/yondelis/drug/34614/