

Yondelis[®] (trabectedin) (Intravenous)

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Yondelis 1 mg single-dose vial for injection: 4 vials every 21 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- **STS/uLMS**
 - 40 billable units every 21 days
- **Myxoid Liposarcoma**
 - 30 billable units every 21 days

III. Initial Approval Criteria ¹

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria ¹

- Left ventricular ejection fraction (LVEF) is within normal limits prior to initiating therapy and will be assessed at regular intervals (e.g., every 3 months) during treatment; **AND**
- Used as single agent therapy; **AND**

Soft Tissue Sarcoma (STS) ‡ Φ ¹⁻⁴

- Patient has unresectable or metastatic liposarcoma or leiomyosarcoma ‡; **AND**
 - Used as subsequent therapy after an anthracycline-containing regimen (e.g., doxorubicin, epirubicin, etc.); **OR**
- Used for myxoid liposarcoma; **AND**

- Patient has one of the following sub-types of soft tissue sarcoma:
 - Retroperitoneal/Intra-Abdominal; **AND**
 - Used as neoadjuvant therapy; **AND**
 - Used for resectable primary or recurrent disease at high risk of becoming metastatic OR if downstaging is needed to facilitate resection (*Note: Systemic therapy is not recommended for low-grade tumors*); **OR**
 - Used as adjuvant therapy; **AND**
 - Used for disease at high risk of becoming metastatic OR if downstaging is needed to facilitate resection (*Note: Systemic therapy is not recommended for low-grade tumors*); **OR**
 - Used for resectable recurrent disease at high risk of becoming metastatic or a history of several recurrences with a high risk for additional local recurrences; **OR**
 - Extremity/Body Wall, Head/Neck; **AND**
 - Used as neoadjuvant therapy for stage III or stage IV (any T, N1, M0) resectable disease with acceptable functional outcomes; **OR**
 - Used as adjuvant therapy; **OR**
 - Used as primary treatment for synchronous stage IV disease with single organ (primarily pulmonary) with limited tumor bulk that is amenable to local therapy; **OR**
 - Used as primary treatment for stage II, III, or IV (any T, N1, M0) resectable disease with adverse functional outcomes; **OR**
 - Used as primary treatment for unresectable disease; **OR**
- Used as palliative therapy; **AND**
 - Patient has one of the following sub-types of soft tissue sarcoma:
 - Rhabdomyosarcoma; **AND**
 - Used as subsequent therapy for advanced or metastatic pleomorphic rhabdomyosarcoma
 - Retroperitoneal/Intra-Abdominal; **AND**
 - Used as subsequent therapy for recurrent unresectable or recurrent stage IV disease
 - Extremity/Body Wall, Head/Neck; **AND**
 - Used as subsequent therapy for advanced or metastatic disease with disseminated metastases
 - Solitary Fibrous Tumor

Uterine Sarcoma ‡^{2,5}

- Patient has uterine leiomyosarcoma (uLMS); **AND**
- Used as subsequent therapy after an anthracycline-containing regimen (e.g., doxorubicin, epirubicin, etc.); **AND**
 - Patient has metastatic, recurrent, or disseminated disease; **OR**
 - Patient has disease that is not suitable for primary surgery

† FDA approved indication(s); ‡ Compendia recommended indication(s); Ⓢ Orphan Drug

IV. Renewal Criteria ¹

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: cardiomyopathy, rhabdomyolysis, hepatotoxicity and/or severe hepatic impairment, capillary leak syndrome (CLS), severe neutropenia/neutropenic sepsis, extravasation resulting in tissue necrosis, etc.; **AND**
- Left ventricular ejection fraction (LVEF) has not had an absolute decrease of $\geq 15\%$ from baseline **OR** is not below the lower limit of normal (LLN) with an absolute decrease of $\geq 5\%$ (LVEF results must be within the previous 3 months)

V. Dosage/Administration ^{1,6,7}

Indication	Dose
Soft Tissue Sarcoma/ Uterine Sarcoma	Administer 1.5 mg/m ² intravenously every 21 days, until disease progression or unacceptable toxicity
Myxoid Liposarcoma	Administer 1.3 mg/m ² intravenously every 21 days, until disease progression or unacceptable toxicity

VI. Billing Code/Availability Information

HCPCS Code:

- J9352 – Injection, trabectedin, 0.1 mg; 1 billable unit = 0.1 mg

NDC:

- Yondelis 1 mg single-dose vial for injection: 59676-0610-xx

VII. References

1. Yondelis [package insert]. Horsham, PA; Janssen Products, LP; June 2020. Accessed July 2022.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) trabectedin. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed July 2022.
3. Demetri GD, von Mehren M, Jones RL, et al. Efficacy and Safety of Trabectedin or Dacarbazine for Metastatic Liposarcoma or Leiomyosarcoma After Failure of Conventional Chemotherapy: Results of a Phase III Randomized Multicenter Clinical Trial. *J Clin Oncol.* 2016;34(8):786-793.
4. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Soft Tissue Sarcoma, Version 2.2022. National Comprehensive Cancer Network, 2022. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed July 2022.
5. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Uterine Neoplasms, Version 1.2022. National Comprehensive Cancer Network, 2022. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed July 2022.
6. Gronchi A, Ferrari S, Quagliuolo V, et al. Histotype-tailored neoadjuvant chemotherapy versus standard chemotherapy in patients with high-risk soft-tissue sarcomas (ISG-ST5 1001): an international, open-label, randomised, controlled, phase 3, multicentre trial. *Lancet Oncol.* 2017 Jun;18(6):812-822. doi: 10.1016/S1470-2045(17)30334-0. Epub 2017 May 9.
7. Hensley ML, Patel SR, von Mehren M, et al. Efficacy and safety of trabectedin or dacarbazine in patients with advanced uterine leiomyosarcoma after failure of anthracycline-based chemotherapy: Subgroup analysis of a phase 3, randomized clinical trial. *Gynecol Oncol.* 2017 Sep;146(3):531-537. doi: 10.1016/j.ygyno.2017.06.018.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C47.0	Malignant neoplasm of peripheral nerves of head, face and neck

ICD-10	ICD-10 Description
C47.10	Malignant neoplasm of peripheral nerves of unspecified upper limb, including shoulder
C47.11	Malignant neoplasm of peripheral nerves of right upper limb, including shoulder
C47.12	Malignant neoplasm of peripheral nerves of left upper limb, including shoulder
C47.20	Malignant neoplasm of peripheral nerves of unspecified lower limb, including hip
C47.21	Malignant neoplasm of peripheral nerves of right lower limb, including hip
C47.22	Malignant neoplasm of peripheral nerves of left lower limb, including hip
C47.3	Malignant neoplasm of peripheral nerves of thorax
C47.4	Malignant neoplasm of peripheral nerves of abdomen
C47.5	Malignant neoplasm of peripheral nerves of pelvis
C47.6	Malignant neoplasm of peripheral nerves of trunk, unspecified
C47.8	Malignant neoplasm of overlapping sites of peripheral nerves and autonomic nervous system
C47.9	Malignant neoplasm of peripheral nerves and autonomic nervous system, unspecified
C48.0	Malignant neoplasm of retroperitoneum
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C49.0	Malignant neoplasm of connective and soft tissue of head, face and neck
C49.10	Malignant neoplasm of connective and soft tissue of unspecified upper limb, including shoulder
C49.11	Malignant neoplasm of connective and soft tissue of right upper limb, including shoulder
C49.12	Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder
C49.20	Malignant neoplasm of connective and soft tissue of unspecified lower limb, including hip
C49.21	Malignant neoplasm of connective and soft tissue of right lower limb, including hip
C49.22	Malignant neoplasm of connective and soft tissue of left lower limb, including hip
C49.3	Malignant neoplasm of connective and soft tissue of thorax
C49.4	Malignant neoplasm of connective and soft tissue of abdomen
C49.5	Malignant neoplasm of connective and soft tissue of pelvis
C49.6	Malignant neoplasm of connective and soft tissue of trunk, unspecified
C49.8	Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9	Malignant neoplasm of connective and soft tissue, unspecified
C54.0	Malignant neoplasm of isthmus uteri
C54.1	Malignant neoplasm of endometrium
C54.2	Malignant neoplasm of myometrium
C54.3	Malignant neoplasm of fundus uteri
C54.8	Malignant neoplasm of overlapping sites of corpus uteri

ICD-10	ICD-10 Description
C54.9	Malignant neoplasm of corpus uteri, unspecified
C55	Malignant neoplasm of uterus, part unspecified
Z85.831	Personal history of malignant neoplasm of soft tissue

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC