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]:

- All Indications**:** 40 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**

Soft Tissue Sarcoma (STS) ‡ [1-4,8,9,1e,3e,6e,8e,9e,21e,23e,24e]

- Used in combination with doxorubicin; **AND**
  - Patient has leiomyosarcoma; **AND**
  - Used as first-line therapy; **AND**
    - Patient has advanced, metastatic, unresectable, or recurrent disease of the extremity/body wall/head-neck; **OR**

        - Patient has advanced, metastatic, unresectable, or residual disease (R2 resection) of the retroperitoneal or intra-abdominal area; **OR**
- Used as single agent therapy; **AND**
    - Patient has liposarcoma or leiomyosarcoma **† Φ**; **AND**
        - Used for unresectable or metastatic disease after an anthracycline-containing regimen (e.g., doxorubicin, liposomal doxorubicin, epirubicin, etc.); **OR**
    - Used as subsequent palliative therapy; **AND**
        - Retroperitoneal/Intra-Abdominal******; **AND**
            - Used for one of the following:
                - Recurrent unresectable or recurrent stage IV disease
                - Used as alternative systemic therapy for unresectable or progressive disease after receiving initial therapy for unresectable or stage IV disease; **OR**
        - Extremity/Body Wall, Head/Neck*****; **AND**
            - Used for advanced or metastatic disease with disseminated metastases

****** For atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDLS) of the extremity, abdominal wall, trunk that was initially diagnosed as ALT and shows evidence of de-differentiation, treat as other soft tissue sarcomas.*

******** For well-differentiated liposarcoma (WDLS-retroperitoneum, paratesticular) with or without evidence of de-differentiation, treat as other soft tissue sarcomas; risk of WDLS progression without de-differentiation is low and therefore single-agent systemic therapy is recommended.*

Uterine Sarcoma ‡ [2,5,8]

- Patient has uterine leiomyosarcoma (uLMS); **AND**
- Patient has advanced, recurrent/metastatic, or inoperable disease; **AND**
    - Used as subsequent therapy after an anthracycline-containing regimen (e.g., doxorubicin, liposomal doxorubicin, epirubicin, etc.); **AND**
        - Used as a single agent therapy; **OR**
    - Used as first-line therapy; **AND**
        - Used in combination with doxorubicin

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA Approved Indication(s); **‡** Compendia Recommended Indication(s); **Φ** 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 ≥ 15% from baseline OR is not below the lower limit of normal (LLN) with an absolute decrease of ≥ 5% (LVEF results must be within the previous 3 months)

V. Dosage/Administration [1,6-8]

Indication	Dose
Soft Tissue Sarcoma	**Single agent therapy** Administer 1.5 mg/m² intravenously every 21 days, until disease progression or unacceptable toxicity **In combination with doxorubicin (leiomyosarcoma ONLY as first-line therapy)** Administer 1.1 mg/m² intravenously, with doxorubicin, every 21 days for up to 6 cycles, followed by single agent maintenance treatment at a dose of 1.1 mg/m² every 21 days until disease progression or unacceptable toxicity
Uterine Sarcoma	**In combination with doxorubicin (first-line therapy)** Administer 1.1 mg/m² intravenously, with doxorubicin, every 21 days for up to 6 cycles, followed by single agent maintenance treatment at a dose of 1.1 mg/m² every 21 days until disease progression or unacceptable toxicity **Single agent therapy (subsequent therapy)** Administer 1.5 mg/m² 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 (STANDARD)

1. Yondelis [package insert]. Horsham, PA; Janssen Products, LP; June 2020. Accessed April 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) trabectedin. National Comprehensive Cancer Network, 2024. 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 April 2024.
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®) Soft Tissue Sarcoma Version 3.2023. National Comprehensive Cancer Network, 2024. 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 NCCN Guidelines, go online to NCCN.org. Accessed April 2024.
5. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Uterine Neoplasms Version 1.2024. National Comprehensive Cancer Network, 2024. 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 NCCN Guidelines, go online to NCCN.org. Accessed April 2024.
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VIII. References (ENHANCED)

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Appendix 1 – Covered Diagnosis Codes

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

ICD-10	ICD-10 Description
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
C54.9	Malignant neoplasm of corpus uteri, unspecified
C55	Malignant neoplasm of uterus, part unspecified
Z85.42	Personal history of malignant neoplasm of other parts of uterus
Z85.831	Personal history of malignant neoplasm of soft tissue

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

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied 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		
Jurisdictio	**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
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
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