# 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]**

- 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 alternative systemic therapy for unresectable or progressive disease of the retroperitoneal or intra-abdominal area after receiving initial therapy for unresectable or stage IV disease; **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 palliative therapy for solitary fibrous tumor; **OR**
    - Used as neoadjuvant therapy; **AND**
        - Patient has myxoid liposarcoma; **AND**
            - Extremity/Body Wall, Head/Neck; **AND**
                - Used for stage III or stage IV (any T, N1, M0) resectable disease with acceptable functional outcomes; **OR**
            - Retroperitoneal/Intra-Abdominal; **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**
        - Patient has myxoid liposarcoma; **AND**
            - Extremity/Body Wall, Head/Neck; **AND**
                - Patient has stage III or stage IV (any T, N1, M0) resectable disease with acceptable functional outcomes; **OR**
                - Patient has stage II, III, or stage IV (any T, N1, M0) resectable disease with adverse functional outcomes; **OR**
                - Patient has unresectable primary disease; **OR**
            - Retroperitoneal/Intra-Abdominal; **AND**
                - Used for disease at high risk of becoming metastatic *(Note: Systemic therapy is not recommended for low-grade tumors)*; **OR**
    - Used as primary treatment; **AND**
        - Patient has myxoid liposarcoma; **AND**
            - Extremity/Body Wall, Head/Neck; **AND**
                - Patient has synchronous stage IV disease with single organ disease (primarily pulmonary) or oligometastatic disease, with limited tumor bulk that is amenable to local therapy; **OR**
                - Patient has stage II, III, or IV (any T, N1, M0) resectable disease with adverse functional outcomes; **OR**
                - Patient has unresectable disease; **OR**
    - Used as subsequent palliative therapy; **AND**

- Rhabdomyosarcoma; **AND**
  - Used for advanced or metastatic pleomorphic rhabdomyosarcoma; **OR**
- Retroperitoneal/Intra-Abdominal******; **AND**
  - Used for recurrent unresectable or recurrent stage IV disease; **OR**
  - 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 or subsequent therapy (if not previously used); **AND**
    - Used in combination doxorubicin

**†** 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 [1,6-9]

| Indication | Dose |
|---|---|
| Soft Tissue Sarcoma | **Single agent therapy**<br>Administer 1.5 mg/m² intravenously every 21 days, until disease progression or unacceptable toxicity<br>**Single agent therapy (myxoid liposarcoma)**<br>Administer 1.3 mg/m² intravenously every 21 days, until disease progression or unacceptable toxicity<br>**In combination with doxorubicin (leiomyosarcoma ONLY as first-line or alternative systemic therapy)**<br>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 or subsequent therapy)**<br>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<br>**Single agent therapy (subsequent therapy)**<br>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


1. Yondelis [package insert]. Horsham, PA; Janssen Products, LP; June 2020. Accessed January 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 January 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®) for 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 Guidelines, go online to NCCN.org. Accessed January 2024.
5. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for 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 Guidelines, go online to NCCN.org. Accessed January 2024.
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-STS 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.
8. Pautier P, Italiano A, Neumann S, et al. Doxorubicin alone versus doxorubicin with trabectedin followed by trabectedin alone as first-line therapy for metastatic or unresectable leiomyosarcoma (LMS-04): a randomised, multicentre, open-label phase 3 trial. Lancet Oncol. 2022 Aug;23(8):1044-1054. doi: 10.1016/S1470-2045(22)00380-1. Epub 2022 Jul 11.
9. Pautier P, Floquet A, Chevreau C, et al. A single-arm multicentre phase II trial of doxorubicin in combination with trabectedin in the first-line treatment for leiomyosarcoma with long-term follow-up and impact of cytoreductive surgery. ESMO Open. 2021 Aug;6(4):100209. doi: 10.1016/j.esmoop.2021.100209. Epub 2021 Jul 26.

## 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 |

| ICD-10 | ICD-10 Description |
|---|---|
| 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 |
| C54.9 | Malignant neoplasm of corpus uteri, unspecified |
| C55 | Malignant neoplasm of uterus, part unspecified |
| D48.1 | Neoplasm of uncertain behavior of connective and other soft tissue |
| Z85.42 | Personal history of malignant neoplasm of other parts of uterus |

| ICD-10 | ICD-10 Description |
|---|---|
| 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 | | |
|---|---|---|
| **Jurisdicti** | **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 |