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**

Soft Tissue Sarcoma (STS) ‡ Φ [1-4]

- Used as single agent therapy; **AND**
  - 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**

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- 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 ‡ [2,5,8]

- Patient has uterine leiomyosarcoma (uLMS); **AND**

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- Patient has advanced, recurrent/metastatic, or inoperable disease; **AND**
  - Used as subsequent therapy after an anthracycline-containing regimen (e.g., 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 [1,6-8]

Indication	Dose
Soft Tissue Sarcoma	Administer 1.5 mg/m² intravenously every 21 days, until disease progression or unacceptable toxicity
Myxoid Liposarcoma	Administer 1.3 mg/m² intravenously every 21 days, until disease progression or unacceptable toxicity
Uterine Sarcoma	In combination with doxorubicin (first-line or subsequent 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

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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 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) trabectedin. National Comprehensive Cancer Network, 2023. 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 2023.
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, 2023. 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 2023.
5. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Uterine Neoplasms, Version 1.2023. National Comprehensive Cancer Network, 2023. 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 2023.
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

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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.

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
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

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ICD-10	ICD-10 Description
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
Z85.831	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

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- Qualified sign language interpreters
- Written information in other formats (large print, audio, accessible electronic formats, other formats)

Provide free language services to people whose primary language is not English, such as:
- Qualified interpreters
- Information written in other languages

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If *you* believe that *we* have failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, sex, sexual orientation, or gender identity, *you* can file a grievance with:

Nondiscrimination Grievance Coordinator
Aspirus Health Plan, Inc.
PO Box 1062
Minneapolis, MN 55440
Phone: 1.866.631.5404 (TTY: 711)
Fax: 763.847.4010
Email: customerservice@aspirushealthplan.com

You can file a grievance in person or by mail, fax, or email. If *you* need help filing a grievance, the Nondiscrimination Grievance Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html.

Language Assistance Services

Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1.866.631.5404 (TTY: 711).

Arabic تنبيه: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية متاحة لك مجاناً . اتصل بن اعلى رقم الهاتف 1.866.631.5404(رقم هاتف الصم والبك : 711)

French: ATTENTION : Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelezle 1.866.631.5404 (ATS : 711).

German: ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zurVerfügung. Rufnummer: 1.866.631.5404 (TTY: 711).

Hindi: _यान द_: य_द आप ि◌हंदी बोलते ह_ तो आपके ि◌लए मु_त म_ भाषा सहायता सेवाएं उपल_ध ह_। 1.866.631.5404 (TTY: 711) पर कॉल कर_।

Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1.866.631.5404 (TTY: 711).

Korean: 주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 1.866.631.5404 (TTY: 711)번으로 전화해 주십시오.

Polish: UWAGA: Jeżeli mówisz po polsku, możesz skorzystać z bezpłatnej pomocy językowej. Zadzwoń pod numer 1.866.631.5404 (TTY: 711).

Russian: ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода.Звоните 1.866.631.5404 (телетайп: 711).

Spanish: ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1.866.631.5404 (TTY: 711).

Tagalog: PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nangwalang bayad. Tumawag sa 1.866.631.5404 (TTY: 711)

Traditional Chinese: 注意：如果您使用繁體中文，您可以免費獲得語言援助服務。請 致電 1.866.631.5404 (TTY:711).

Vietnamese: CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 1.866.631.5404 (TTY: 711).

Pennsylvania Dutch: Wann du Deitsch (Pennsylvania German / Dutch) schwetzscht, kannscht du mitaus Koschte ebbergricke, ass dihr helft mit die englisch Schprooch. Ruf selli Nummer uff: Call 1.866.631.5404 (TTY: 711).

Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັ້ງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1.866.631.5404 (TTY:711).

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