Clinical Policy: Trabectedin (Yondelis)

Reference Number: PA.CP.PHAR.204
Effective Date: 01/2018
Last Review Date: 01/2026

Description
Trabectedin (Yondelis®) is an alkylating drug.

FDA Approved Indication(s)
Yondelis is indicated for the treatment of patients with unresectable or metastatic liposarcoma (LPS) or leiomyosarcoma (LMS) who received a prior anthracycline-containing regimen.

Policy/Criteria
It is the policy of PA Health & Wellness that Yondelis is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Soft Tissue Sarcoma (must meet all)**:**

1. Diagnosis of one of the following soft tissue sarcomas (STS) (a-g):
   a. STS that is unresectable, progressive, advanced or metastatic;
   b. Leiomyosarcoma;
   c. Angiosarcoma;
   d. Advanced/metastatic pleomorphic rhabdomyosarcoma;
   e. Myxoid liposarcoma (LPS) that is one of the following (i-v):
      i. Resectable;
      ii. High risk for metastatic disease;
      iii. Local recurrence;
      iv. Unresectable primary disease;
      v. Stage IV disease that is amendable to local therapy;
   f. Solitary fibrous tumor, epithelioid hemangioendothelioma, or dedifferentiated liposarcoma with or without concurrent well-differentiated liposarcoma;
   g. Other NCCN recommendations listed as category 1, 2A, or 2B;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. If uterine leiomyosarcoma (uLMS), prescribed in one of the following ways (a, b or c):
   a. As a single agent AND member has received a prior anthracycline-containing regimen (e.g., doxorubicin);
   b. In combination with doxorubicin;
   c. Other NCCN recommendations listed as category 1, 2A, or 2B;
5. Request meets one of the following (a or b):
   a. Dose does not exceed 1.5 mg/m^2 body surface area every 3 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Soft Tissue Sarcoma (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
    a. New dose does not exceed 1.5 mg/m^2 body surface area every 3 weeks;
    b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*)

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies; **Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
LMS: leiomyosarcoma
LPS: liposarcoma
STS: soft tissue sarcoma
uLMS: uterine leiomyosarcoma

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
uLMS - examples of anthracycline-containing regimens: doxorubicin ± gemcitabine, olaratumab, fosfamide, or dacarbazine; epirubicin; liposomal doxorubicin	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): Known hypersensitivity to trabectedin
- Boxed warning(s): None reported

Appendix D: Types and Examples of STSs

Examples are drawn from the National Comprehensive Center Network (NCCN) Soft Tissue Sarcoma Guideline, which cites the 2020 World Health Organization classification of tumors, and the Yondelis compendium.

- Smooth muscle tumors - LMS

- Vascular tumors - angiosarcoma
- Myo/fibroblastic tumors - solitary fibrous tumor
- Skeletal muscle tumors - rhabdomyosarcoma
- Adipocytic tumors – myxoid LPS
  - Begin in the adipose cells, usually occurring in the thigh and sometimes in the outer torso or buttocks
  - Myxoid LPS has a higher risk of metastasis to the spine compared to other STSs

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
LPS, LMS	1.5 mg/m^2 (body surface area) as a 24-hour IV infusion every 21 days (3 weeks), until disease progression or unacceptable toxicity	Varies

V. Product Availability

Single-dose vial with powder for injection: 1 mg

VI. References

1. Yondelis Prescribing Information. Horsham, PA: Janssen Products, LP; June 2020. Available at: http://www.yondelis.com. Accessed November 6, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: www.nccn.org. Accessed November 19, 2025.
3. National Comprehensive Cancer Network. Soft Tissue Sarcoma Version 1.2025. Available at: www.nccn.org. Accessed November 19, 2025.
4. National Comprehensive Cancer Network. Uterine Neoplasms Version 2.2026. Available at: www.nccn.org. Accessed November 19, 2025.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9352	Injection, trabectedin, 0.1 mg

Reviews, Revisions, and Approvals	Date
Added age requirement as safety and efficacy have not been established in pediatric patients. Removed criteria around specific FDA/NCCN uses that are under the purview of the provider, and added prescriber requirement to ensure appropriate use. Require that use be for palliative therapy or for metastatic or unresectable disease Re-auth: Modified requirement for no disease progression or unacceptable toxicity to requirement for positive response to therapy. Added max dosing criteria. References reviewed and updated	

Reviews, Revisions, and Approvals	Date
1Q 2019 annual review; coverage of STS is expanded to encompass STS subtypes of non-specific histologies per NCCN; references reviewed and updated.	01/2019
1Q 2020 annual review: references reviewed and updated.	01/2020
1Q 2021 annual review: references reviewed and updated.	01/2021
1Q 2022 annual review: added myxoid LPS indication supported as category 2A in NCCN compendium; added Appendix D with STS examples; references reviewed and updated.	01/2022
1Q 2023 annual review: no significant changes; references reviewed and updated.	01/2023
1Q 2024 annual review: for uLMS, clarified Yondelis prescribed as single agent for those who has received a prior anthracycline-containing regimen and added option for usage of Yondelis in combination with doxorubicin; references reviewed and updated.	01/2024
1Q 2025 annual review: for myxoid LPS, added option for unresectable primary disease and Stage IV disease that is amendable to local therapy; references reviewed and updated.	01/2025
1Q 2026 annual review: added the following sub-types of STS without requiring disease to be unresectable or metastatic: solitary fibrous tumor, epithelioid hemangioendothelioma, or dedifferentiated liposarcoma with or without concurrent well-differentiated liposarcoma per NCCN; extended initial approval duration from 6 to 12 months for this maintenance medication for a chronic condition; references reviewed and updated.	01/2026