# Clinical Policy: Topotecan (Hycamtin)

Reference Number: CP.PHAR.64
Effective Date: 06.01.11
Last Review Date: 05.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

## Description

Topotecan (Hycamtin®) is a topoisomerase inhibitor.

## FDA Approved Indication(s)

Hycamtin capsules are indicated for the treatment of relapsed small cell lung cancer in patients with a prior complete or partial response and who are at least 45 days from the end of first-line chemotherapy.

Hycamtin for injection is indicated:

- As a single agent for the treatment of patients with metastatic carcinoma of the ovary after disease progression on or after initial or subsequent chemotherapy
- As a single agent for the treatment of patients with small cell lung cancer with platinum-sensitive disease who progressed at least 60 days after initiation of first-line chemotherapy
- In combination with cisplatin for the treatment of patients with Stage IV-B, recurrent, or persistent carcinoma of the cervix not amenable to curative treatment

## Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation® that Hycamtin is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Ovarian Cancer** (must meet all)**:**

1. Diagnosis of ovarian cancer (including epithelial carcinoma, mucinous carcinoma, clear cell carcinoma, endometrioid carcinoma, low-grade serious carcinoma, and carcinosarcoma), fallopian tube cancer, or primary peritoneal cancer;
2. Request is for topotecan for injection;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Disease progression on or after initial or subsequent chemotherapy;
6. Prescribed in one of the following ways (a or b):
   a. As a single agent;
   b. In combination with bevacizumab or sorafenib (off-label);
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 1.5 mg/m$^2$ per day for 5 consecutive days every 21 days;

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**
**Medicaid/HIM –** 6 months
**Commercial –** 6 months or to the member's renewal date, whichever is longer

**B. Small Cell Lung Cancer** (must meet all)**:**

1. Diagnosis of small cell lung cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member has received prior chemotherapy;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed the following:
      i. Injection: 1.5 mg/m$^2$ per day IV for 5 consecutive days every 21 days;
      ii. Capsule: 2.3 mg/m$^2$ per day orally for 5 consecutive days every 21 days;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label *use (prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**
**Medicaid/HIM –** 6 months
**Commercial –** 6 months or to the member's renewal date, whichever is longer (injection); 12 months or duration of request, whichever is less (capsule)

**C. Cervical Cancer** (must meet all)**:**

1. Diagnosis of cervical cancer;
2. Request is for topotecan for injection;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Prescribed in one of the following ways (a or b):
   a. In combination with cisplatin or paclitaxel;
   b. As a single agent as second-line or subsequent therapy;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 0.75 mg/m$^2$ per day on days 1-3 every 21 days;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**
**Medicaid/HIM –** 6 months
**Commercial –** 6 months or to the member's renewal date, whichever is longer

**D. NCCN Recommended Uses (off-label)** (must meet all)**:**

1. Prescribed for one of the following diagnoses:
   a. Request is for topotecan for injection:
      i. Ewing sarcoma, and prescribed as a second line therapy in combination with cyclophosphamide;

ii. Osteosarcoma, and prescribed as a second line therapy in combination with cyclophosphamide;
iii. Leptomeningeal metastases, and route of administration is intrathecal;
iv. Non-pleomorphic rhabdomyosarcoma, and prescribed as a single agent or in combination with cyclophosphamide;
v. Endometrial carcinoma, and prescribed as a single agent;

b. Request is for topotecan for injection or topotecan capsules:
i. Merkel cell carcinoma, and member has contraindications to checkpoint immunotherapy (e.g., avelumab, pembrolizumab, nivolumab);

2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Dose is within FDA maximum limit for any FDA approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).**
**Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**
**Medicaid/HIM –** 6 months
**Commercial –** 6 months or to the member's renewal date, whichever is longer (injection); 12 months or duration of request, whichever is less (capsule)

**E. Other diagnoses/indications**

Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

## II. Continued Therapy

**A. All Indications in Section I** (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Hycamtin for a covered indication and has received this medication for at least 30 days;
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 the following (i, ii, or iii):
      i. Ovarian cancer: 1.5 mg/m$^2$ per day IV for 5 consecutive days every 21 days;
      ii. Small cell lung cancer: 1.5 mg/m$^2$ per day IV *or* 2.3 mg/m$^2$/day orally for 5 consecutive days repeated every 21 days;
      iii. Cervical cancer: 0.75 mg/m$^2$ per day IV on days 1-3 every 21 days;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**
**Medicaid/HIM –** 12 months
**Commercial –** 6 months or to the member's renewal date, whichever is longer (injection); 12 months or duration of request, whichever is less (capsule)

**B. Other diagnoses/indications** (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   **Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

## III. Diagnoses/Indications for which coverage is NOT authorized:

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid, or evidence of coverage documents.

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network

*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 for all relevant lines of business and may require prior authorization.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| **Examples* of therapies for ovarian cancer**: paclitaxel, carboplatin, cisplatin, doxorubicin, ifosfamide, bevacizumab | Varies | Varies |
| **Examples* of therapies for small cell lung cancer**: cisplatin, carboplatin, etoposide, atezolizumab, durvalumab, irinotecan | Varies | Varies |
| **Examples* of therapies for cervical cancer**: cisplatin, carboplatin, pembrolizumab, bevacizumab, nivolumab, paclitaxel, docetaxel, fluorouracil, gemcitabine, ifosfamide, irinotecan, mitomycin, pemetrexed, vinorelbine, tisotumab vedotin-tftv | Varies | Varies |
| **Examples* of therapies for Ewing sarcoma and osteosarcoma**: pembrolizumab, dasatinib, pazopanib, ivosidenib | 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.*
**Examples are not all-inclusive and may be used alone or in various combination regimens; refer to NCCN guidelines for additional detail*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): history of severe hypersensitivity reactions to topotecan
- Boxed warning(s): myelosuppression

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| Ovarian cancer | IV infusion dosage:<br>1.5 mg/m$^2$ IV over 30 minutes daily for 5 consecutive days, starting on Day 1 of a 21-day course | 4 mg/dose if IV infusion, otherwise refer to regimen |
| Small cell lung cancer | IV infusion dosage:<br>1.5 mg/m$^2$ IV over 30 minutes daily for 5 consecutive days, starting on Day 1 of a 21-day course<br><br>Oral dosage: 2.3 mg/m$^2$/day orally once daily for 5 consecutive days repeated every 21 days | 4 mg/dose if IV infusion, otherwise refer to regimen |
| Cervical cancer | IV infusion dosage:<br>0.75 mg/m$^2$ IV over 30 minutes daily on Days 1, 2, and 3 repeated every 21 days in combination with cisplatin 50 mg/m$^2$ on Day 1 | 4 mg/dose if IV infusion, otherwise refer to regimen |

## VI. Product Availability

- Capsules: 0.25 mg, 1 mg
- Lyophilized powder in single use vial for injection: 4-mg (free base)

## VII. References

1. Hycamtin for Injection Prescribing Information. East Hanover, NJ: Novartis; October 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020671s024lbl.pdf. Accessed January 28, 2022.
2. Hycamtin capsules Prescribing Information. East Hanover, NJ: Novartis; September 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/020981s008lbl.pdf. Accessed January 28, 2022.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed January 28, 2022.

## 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 |
|---|---|
| J8705 | Topotecan, oral, 0.25 mg |
| J9351 | Injection, topotecan, 0.1 mg |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| 2Q 2018 annual review: HIM added; summarized NCCN and FDA approved uses for improved clarity; added specialist involvement in care; added continuity of care statement; added age; removed lab requirements pertaining to baseline neutrophil and platelet counts; off-label NCCN recommended uses (e.g., bone cancer, CNS cancers, etc.): updated to include only category 2A (removed 2b); added requirement that request is for the injectable formulation, added dosing statement and initial approval duration of 6 months; references reviewed and updated. | 02.13.18 | 05.18 |
| 2Q 2019 annual review: Commercial line of business added; capsules added as an option for Merkel cell carcinoma and intrathecal route notated for leptomeningeal metastasis per NCCN; references reviewed and updated. | 12.19.19 | 05.19 |
| 2Q 2020 annual review: no significant changes; references reviewed and updated. | 02.11.20 | 05.20 |
| 2Q 2021 annual review: no significant changes; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated. | 02.12.21 | 05.21 |
| 2Q 2022 annual review: revisions made per FDA label and/or NCCN recommendations – for ovarian cancer, expanded coverable diagnoses to include additional types of ovarian cancer as well as fallopian tube and primary peritoneal cancer and added requirement for use as a single agent or in combination with bevacizumab or sorafenib; for cervical cancer, added requirement for use in combination with cisplatin or paclitaxel, or as a single agent as second-line or subsequent therapy; for off-label uses, removed primary CNS lymphoma and added specific requirements for use in Ewing sarcoma, osteosarcoma, endometrial sarcoma, and rhabdomyosarcoma; modified Commercial approval duration for capsules from "Length of Benefit" to "12 months or duration of request, whichever is less"; references reviewed and updated. | 01.28.22 | 05.22 |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health

plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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**Note: For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.