Clinical Policy: Topotecan (Hycamtin)

Reference Number: PA.CP.PHAR.64
Effective Date: 01/2018
Last Review Date: 04/2023

Coding Implications
Revision Log

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 PA Health & Wellness 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. Requested dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 6 months

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

Approval duration: 6 months

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 on days 1-3 every 21 days;
   b. Requested dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use *(prescriber must submit supporting evidence).*

Approval duration: 6 months

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 as second-line or subsequent therapy, 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);
   c. Meets conditions of a NCCN category 1, 2A, or 2B recommendation;
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).*

Approval duration: 6 months

E. Other diagnoses/indications

1. Refer to PA.CP.PMN.53.

II. Continued Therapy

A. All Indications in Section I (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.LTSS.PHAR.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 the following (i, ii, or iii):
      i. Ovarian cancer: 1.5 mg/m^2/day IV for 5 consecutive days every 21 days;
      ii. Small cell lung cancer: 1.5 mg/m^2/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 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).*

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.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53.

III. 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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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, vinrelbine, tisotumab vedontin-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

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Ovarian cancer	IV infusion dosage: 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: 1.5 mg/m^2 IV over 30 minutes daily for 5 consecutive days, starting on Day 1 of a 21-day course 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: 0.75 mg/m^2 IV over 30 minutes 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

V. Product Availability

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

VI. 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 February 7, 2023.
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 February 7, 2023.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed February 7, 2023.

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
Policy created	03.13.18	04.18.18
2Q 2019 annual review: capsules added as an option for Merkel cell carcinoma and intrathecal route notated for leptomeningeal metastasis per NCCN; references reviewed and updated.	04.2019	
2Q 2020 annual review: references reviewed and updated.	04/2020	
2Q 2021 annual review: no significant changes; preferences reviewed and updated.	04/2021	
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; references reviewed and updated.	04/2022	
2Q 2023 annual review: updated off-label criteria for endometrial carcinoma to include “as second line or subsequent therapy” per NCCN compendium; references reviewed and updated.	04/2023	