VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable) – Topotecan Products Utilization Management Medical Policy
- Hycamtin® (topotecan intravenous infusion – Novartis, generics)

REVIEW DATE: 02/05/2025

OVERVIEW

Topotecan injection, a topoisomerase inhibitor, is indicated for the treatment of patients with:[1]

- **Cervical cancer**, stage IV-B, recurrent, or persistent disease which is not amenable to curative treatment, in combination with cisplatin.
- **Metastatic ovarian cancer**, after disease progression on or after initial or subsequent chemotherapy, as a single agent.
- **Small cell lung cancer** (SCLC), platinum-sensitive disease that progressed at least 60 days after initiation of first-line chemotherapy, as a single agent.

Guidelines

Topotecan is included in a variety of National Comprehensive Cancer Network (NCCN) guidelines:

- **Bone cancer** (version 1.2025 – August 20, 2024) clinical practice guidelines recommend topotecan in combination with cyclophosphamide, as second-line therapy for patients with relapsed/refractory, or metastatic osteosarcoma and Ewing sarcoma (both category 2A), and dedifferentiated chondrosarcoma, high-grade undifferentiated pleomorphic sarcoma, and mesenchymal chondrosarcoma (category 2B).[2,7]
- **Central nervous system cancers** (version 4.2024 – January 21, 2025) clinical practice guidelines recommend topotecan as a single agent for the treatment of brain metastases in patients with small cell lung cancer (category 2B).[2,8] In addition, the guidelines recommend intra-cerebrospinal fluid topotecan for the treatment of leptomeningeal metastases (category 2A).
- **Cervical cancer** (version 1.2025 – December 19, 2024) clinical practice guidelines recommend topotecan as first-line, second-line, or subsequent therapy for patients with local/regional recurrence, stage IV-B disease, or distant metastases in combination with paclitaxel and bevacizumab (category 1), or in combination with paclitaxel or cisplatin (category 2A); or as a single agent in second-line and subsequent therapy.[2,5] It is also recommended as first-line, second-line and subsequent therapy for patients with persistent, recurrent, or metastatic small cell neuroendocrine carcinoma of the cervix (NECC) in combination with paclitaxel and bevacizumab. Topotecan can be used in combination with paclitaxel or cisplatin, or as a single agent (category 2A) for second-line or subsequent therapy of NECC.
- **Merkel cell carcinoma** (version 1.2025 – January 17, 2025) clinical practice guidelines recommend topotecan as a treatment option for patients with regional or distant metastatic disease who have contraindications to checkpoint immunotherapy (Bavencio® [avelumab intravenous infusion], Keytruda® [pembrolizumab intravenous infusion], and Opdivo® [nivolumab intravenous infusion]); or have progressed on checkpoint immunotherapy (category 2A).[2,10]
- **Neuroblastoma** (version 2.2024 – July 2, 2024) clinical practice guidelines recommend topotecan, in combination with cyclophosphamide, for induction therapy of patients with high-risk disease (category 2A).[2,12] Topotecan, in combination with cyclophosphamide, is also recommended for the subsequent treatment of intermediate risk disease if adequate response on imaging has not been achieved and undifferentiated viable tumor remains (category 2A).
- **Ovarian cancer** (version 3.2024 – July 15, 2024) clinical practice guidelines recommend topotecan, as a single agent or in combination with bevacizumab or sorafenib, for the treatment of

recurrent or persistent platinum-resistant epithelial ovarian cancer, fallopian tube cancer, and peritoneal cancer.[2,3] Treatment of clinical relapse is a category 2A recommendation and immediate treatment of biochemical relapse is category 2B recommendation.

- **Pediatric central nervous system cancers** (version 2.2025 – January 17, 2025) clinical practice guidelines recommend topotecan, in combination with temozolomide, for the treatment of medulloblastoma (category 2A).[2,14]
- **SCLC** (version 4.2025 – January 13, 2025) clinical practice guidelines recommend topotecan as a single agent for patients with a performance status of 0 to 2 and relapse following complete or partial response, or stable disease with initial treatment; or for primary progressive disease (category 2A).[2,4]
- **Soft tissue sarcoma** (version 4.2024 – November 21, 2024) clinical practice guidelines recommend topotecan as a single agent or in combination with cyclophosphamide for the treatment of non-pleomorphic rhabdomyosarcoma (category 2A).[2,11]
- **Uterine cancer** (version 1.2025 – December 16, 2024) clinical practice guidelines recommend topotecan as a single agent for the treatment of recurrent or metastatic endometrial carcinoma (category 2A).[2,6]
- **Vaginal cancer** (version 3.2025 – December 16, 2024) clinical practice guidelines recommend topotecan as first-line treatment in combination with paclitaxel with or without bevacizumab, or cisplatin, and as a single agent for the subsequent treatment of recurrent or metastatic disease (category 2A).[2,13]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of topotecan. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with topotecan as well as the monitoring required for adverse events and long-term efficacy, approval requires topotecan to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of topotecan is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. Cervical Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient meets ONE of the following (i or ii):
  - **i.** Patient has persistent or recurrent disease; OR
  - **ii.** Patient has metastatic disease; AND
- **C)** Medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 1.5 mg/m^2 administered intravenously for up to 5 days in each 21-day cycle.

2. **Ovarian, Fallopian Tube, and Primary Peritoneal Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 18 years or age; AND
   - **B)** Patient has persistent or recurrent disease; AND
   - **C)** The cancer is platinum-resistant; AND
   - **D)** Medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 1.5 mg/m^2 administered intravenously for up to 5 days in each 21-day cycle.

3. **Small Cell Lung Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets ONE of the following (i or ii):
     - **i.** Patient has relapsed disease; OR
     - **ii.** Patient has primary progressive disease; AND
   - **C)** Medication will be used as a single agent; AND
   - **D)** Medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 1.5 mg/m^2 administered intravenously for up to 5 days in each 21-day cycle.

Other Uses with Supportive Evidence

4. **Bone Cancer.** Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
   - **A)** Patient has ONE of the following (i, ii, iii, iv, or v):
     - **i.** Osteosarcoma; OR
     - **ii.** Ewing sarcoma; OR
     - **iii.** Dedifferentiated chondrosarcoma; OR
     - **iv.** High-grade undifferentiated pleomorphic sarcoma; OR
     - **v.** Mesenchymal chondrosarcoma; AND
   - **B)** Patient has relapsed, refractory, or metastatic disease; AND
   - **C)** Medication is used second-line; AND
   - **D)** Medication is used in combination with cyclophosphamide; AND
   - **E)** Medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 1.5 mg/m^2 administered intravenously for up to 5 days in each 21-day cycle.

5. **Brain Metastases**. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has small cell lung cancer; AND
   - **C)** Medication will be used as a single agent; AND
   - **D)** Medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve up to 1.5 mg/m^2 administered intravenously for up to 5 days in each 21-day cycle.

6. **Endometrial Carcinoma**. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has recurrent or metastatic disease; AND

C) Medication will be used as a single agent; AND
D) Medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 1.5 mg/m^2 administered intravenously for up to 5 days in each 21-day cycle.

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7. Leptomeningeal and Spinal Metastases. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Medication will be administered intraventricularly; AND
C) Medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 0.4 mg administered intraventricularly no more frequently than two times a week.

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8. Medulloblastoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient has recurrent or progressive disease; AND
B) Medication will be given in combination with temozolomide; AND
C) Medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 0.75 mg/m^2 administered intravenously for up to 5 times in each 28-day cycle.

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9. Merkel Cell Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
A) Patient is ≥ 18 years of age; AND
B) Patient has regional or distant metastatic disease; AND
C) Patient meets ONE of the following (i or ii):
  i. Patient has contraindications to checkpoint immunotherapy; OR
    Note: Checkpoint immunotherapy includes Bavencio (avelumab intravenous infusion), Keytruda (pembrolizumab intravenous infusion), and Opdivo (nivolumab intravenous infusion).
  ii. Patient has progressed on checkpoint immunotherapy; AND
    Note: Checkpoint immunotherapy includes Bavencio, Keytruda, and Opdivo.
D) Medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 1.5 mg/m^2 administered intravenously for up to 5 days in each 21-day cycle.

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10. Neuroblastoma. Approve for the duration noted if the patient meets ALL of the following (A, B, and C):
A) Patient meets ONE of the following (i or ii):
  i. Approve for 3 months if the patient meets BOTH of the following (a and b):
    a) Patient has high-risk disease; AND
    b) Medication is used for primary treatment; OR
  ii. Approve for 6 months if the patient meets BOTH of the following (a and b):
    a) Patient has intermediate-risk disease; AND
    b) Medication is used for subsequent treatment; AND
B) Medication is used in combination with cyclophosphamide; AND

C) Medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 1.2 mg/m^2 administered intravenously for up to 5 days in each 21-day cycle.

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11. Rhabdomyosarcoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Patient has non-pleomorphic rhabdomyosarcoma; AND
C) Medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 1.5 mg/m^2 administered intravenously for up to 5 days in each 21-day cycle.

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12. Vaginal Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Patient has recurrent or metastatic disease; AND
C) Medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 1.5 mg/m^2 administered intravenously for up to 5 days in each 21-day cycle.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of topotecan is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Hycamtin® intravenous infusion [prescribing information]. East Hanover, NJ: Novartis; October 2019.
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8. The NCCN Central Nervous System Cancers Clinical Practice Guidelines (version 4.2024 – January 21, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed January 27, 2025.
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14. The NCCN Pediatric Central Nervous System Clinical Practice Guidelines in Oncology (version 2.2025 – January 17, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed January 27, 2025.
15. Le Teuff G, Castaneda-Heredia A, Dufour C, et al. Phase II study of temozolomide and topotecan (TOTEM) in children with relapsed of refractory extracranial and central nervous system tumors uncluding medulloblastoma with post hoc Bayesian analysis: A European ITCC study. *Pediatr Blood Cancer*. 2020;67(1):e28032.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	01/18/2023
Annual Revision	**Merkel Cell Carcinoma.** Patient has progressed on checkpoint immunotherapy added as an additional option for approval. Patient has contraindications to checkpoint immunotherapy changed to an option for approval.	01/17/2024
Annual Revision	**Endometrial Carcinoma:** Descriptor "high-risk" removed from requirement that the patient has recurrent or metastatic disease. **Medulloblastoma:** Added new condition of approval. **Merkel Cell Carcinoma:** Added "regional" to requirement that the patient has regional or distant metastatic disease. **Neuroblastoma:** Added new condition of approval. **Vaginal Cancer:** Added new condition of approval.	02/05/2025