



POLICY: Oncology – Topotecan injection for intravenous use (Hycamtin® – Novartis, generics)

DATE REVIEWED: 12/18/2019

OVERVIEW

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

- 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 who progressed at least 60 days after initiation of first-line chemotherapy, as a single agent;
- Stage IV-B, recurrent, or persistent cervical cancer which is not amenable to curative treatment, in combination with cisplatin.¹

Guidelines

The National Comprehensive Cancer Network (NCCN) ovarian cancer (Version 2.2019 – September 17, 2019) clinical practice guidelines recommend topotecan, as a single agent or in combination with bevacizumab or Nexavar® (sorafenib tablet), 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.

The NCCN SCLC (Version 2.2020 – November 15, 2019) clinical practice guidelines recommend topotecan as a single agent for patients with a performance status of 0-2 and relapse within 6 months following complete or partial response, or stable disease with initial treatment; or for primary progressive disease.^{2,4}

The NCCN cervical cancer (Version 5.2019 – September 16, 2019) clinical practice guidelines recommend topotecan as first- or second-line therapy for patients with local/regional recurrence, stage IVB disease, or distant metastases.^{2,5} Topotecan can be used in combination with paclitaxel with or without bevacizumab, in combination with cisplatin, or as a single agent for second-line therapy (category 2B recommendation).

The NCCN uterine cancer (Version 4.2019 – September 16, 2019) clinical practice guidelines recommend topotecan as a single agent for the treatment of recurrent, metastatic, or high-risk endometrial carcinoma.^{2,6}

The NCCN bone cancer (Version 1.2020 – August 12, 2019) 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}

The NCCN central nervous system (CNS) cancers (Version 3.2019 – October 18, 2019) clinical practice guidelines recommend topotecan as a single agent for the treatment of relapsed or refractory primary CNS lymphoma and recurrent brain metastases in patients with small cell lung cancer.^{2,8} In addition, the guidelines recommend intra-cerebrospinal fluid topotecan for the treatment of leptomeningeal metastases.

The NCCN Merkel cell carcinoma (Version 1.2020 – October 2, 2019) clinical practice guidelines recommend topotecan as a treatment option for patients with distant metastatic disease who have

contraindications to checkpoint immunotherapy (Bavencio® [avelumab injection for intravenous use], Keytruda® [injection for intravenous use], and Opdivo® [injection for intravenous use]).^{2,10}

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 indication(s). 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).

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.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. Ovarian, Fallopian Tube, and Primary Peritoneal Cancer. Approve for 1 year if the patient meets the following criteria (A, B, and C):

- A) The patient has persistent or recurrent disease; AND
- B) The cancer is platinum-resistant; AND
- C) Topotecan is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Each individual dose must not exceed 1.5 mg/m² administered intravenously for up to 5 days in each 21-day cycle.¹

2. Small Cell Lung Cancer. Approve for 1 year if the patient meets the following criteria (A, B, and C):

- A) The patient meets one of the following (i or ii):
 - i. The patient has relapsed disease; OR
 - ii. The patient has primary progressive disease; AND
- B) Topotecan will be used as a single agent; AND
- C) Topotecan is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Each individual dose must not exceed 1.5 mg/m² administered intravenously for up to 5 days in each 21-day cycle.¹

3. Cervical Cancer. Approve for 1 year if the patient meets the following criteria (A and B):

- A) The patient meets one of the following (i or ii):
 - i. The patient has local/regional recurrence; OR
 - ii. The patient has distant metastases; AND
- B) Topotecan is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Each individual dose must not exceed 1.5 mg/m² administered intravenously for up to 5 days in each 21-day cycle.¹

Other Uses with Supportive Evidence

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- 4. Endometrial Carcinoma.** Approve for 1 year if the patient meets the following criteria (A, B, and C):
- A) The patient has recurrent, metastatic, or high-risk disease; AND
 - B) Topotecan will be used as a single agent; AND
 - C) Topotecan is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Each individual dose must not exceed 1.5 mg/m² administered intravenously for up to 5 days in each 21-day cycle.¹

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- 5. Rhabdomyosarcoma.** Approve for 1 year if the patient meets the following criteria (A and B):
- A) The patient has non-pleomorphic rhabdomyosarcoma; AND
 - B) Topotecan is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Each individual dose must not exceed 1.5 mg/m² administered intravenously for up to 5 days in each 21-day cycle.¹

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- 6. Bone Cancer.** Approve for 1 year if the patient meets the following criteria (A, B, C, D, and E):
- A) The 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) The patient has relapsed, refractory, or metastatic disease; AND
 - C) Topotecan is used second-line; AND
 - D) Topotecan is used in combination with cyclophosphamide; AND
 - E) Topotecan is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Each individual dose must not exceed 1.5 mg/m² administered intravenously for up to 5 days in each 21-day cycle.¹

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- 7. Primary Central Nervous System Lymphoma.** Approve for 1 year if the patient meets the following criteria (A, B, and C):
- A) The patient has relapsed or refractory disease; AND
 - B) Topotecan will be used as a single agent; AND
 - C) Topotecan is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Each individual dose must not exceed 1.5 mg/m² administered intravenously for up to 5 days in each 21-day cycle.¹

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- 8. Brain Metastases.** Approve for 1 year if the patient meets the following criteria (A, B, C, and D):
- A) The patient has recurrent disease; AND

- B) The patient has small cell lung cancer; AND
- C) Topotecan will be used as a single agent; AND
- D) Topotecan is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Each individual dose must not exceed 1.5 mg/m² administered intravenously for up to 5 days in each 21-day cycle.¹

9. Leptomeningeal and Spinal Metastases. Approve for 1 year if the patient meets the following criteria (A and B):

- A) Topotecan will be administered intraventricularly; AND
- B) Topotecan is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Each individual dose must not exceed 0.4 mg administered intraventricularly no more frequently than two times a week.⁹

10. Merkel Cell Carcinoma. Approve for 1 year if the patient meets the following criteria (A, B, and C):

- A) The patient has distant metastatic disease; AND
- B) The patient has contraindications to checkpoint immunotherapy.
Note: Checkpoint immunotherapy includes Bavencio[®] (avelumab injection for intravenous use), Keytruda[®] (injection for intravenous use), and Opdivo[®] (injection for intravenous use); AND
- C) Topotecan is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing regimen: Each individual dose must not exceed 1.5 mg/m² administered intravenously for up to 5 days in each 21-day cycle.¹

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Topotecan has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

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 injection for intravenous use [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals; October 2019.
2. The NCCN Drugs & Biologics Compendium. © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed on November 20, 2019. Search term: topotecan.
3. The NCCN Ovarian Cancer Clinical Practice Guidelines (Version 2.2019 – September 17, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed November 20, 2019.
4. The NCCN Small Cell Lung Cancer Clinical Practice Guidelines (Version 2.2020 – November 15, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed November 21, 2019.
5. The NCCN Cervical Cancer Clinical Practice Guidelines (Version 5.2019 – September 16, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed November 21, 2019.
6. The NCCN Uterine Cancer Clinical Practice Guidelines (Version 4.2019 – September 16, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed November 22, 2019.
7. The NCCN Bone Cancer Clinical Practice Guidelines (Version 1.2020 – August 12, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed November 22, 2019.

8. The NCCN Central Nervous System Cancers Clinical Practice Guidelines (Version 3.2019 – October 18, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed November 22, 2019.
9. Groves MD, Glantz MJ, Chamberlain MC, et al. A multicenter phase II trial of intrathecal topotecan in patients with meningeal malignancies. *Neuro Oncol.* 2008;208-215.
10. The NCCN Merkel Cell Carcinoma Clinical Practice Guidelines (Version 1.2020 – October 2, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: <http://www.nccn.org>. Accessed November 25, 2019.

HISTORY

Type of Revision	Summary of Changes	Date Reviewed
New Policy	--	12/18/2019