Medical Drug Clinical Criteria

Subject:	Torisel (temsirolimus)		
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Overview

This document addresses the use of Torisel (temsirolimus). Torisel is an inhibitor of mammalian target of rapamycin (mTOR) primarily used to treat renal cell carcinoma.

Torisel is FDA approved for advanced renal cell carcinoma (RCC). It was approved based on results from a phase 3 trial of patients with previously untreated advanced RCC (clear cell and non-clear cell histologies) (Hudes 2007). Patients in this study had 3 or more of 6 pre-selected prognostic risk factors (less than one year from time of initial renal cell carcinoma diagnosis to randomization, Karnofsky performance status of 60 or 70, hemoglobin less than the lower limit of normal, corrected calcium of greater than 10 mg/dL, lactate dehydrogenase >1.5 times the upper limit of normal, more than one metastatic organ site).

Temsirolimus is a useful in certain circumstances option for non-clear cell Renal cell cancer (nccRCC); it has a category 1 designation for patients with poor-risk nccRCC and a category 2A designation for patients with favorable-/intermediate-risk nccRCC. NCCN also recommends Torisel in certain types of soft tissue sarcoma (PEComa, recurrent angiomyolipoma, and lymphangioleiomyomatosis, rhabdomyosarcoma) and for advanced, recurrent, or metastatic endometrial carcinoma.

Other Uses
The National Comprehensive Cancer Network® (NCCN) provides additional recommendations. The NCCN Panel for Kidney Cancer has included first-line temsirolimus as a category 3, useful in certain circumstances option for patients with poor- and intermediate-risk ccRCC. Also the Panel considers temsirolimus a category 2B, useful in certain circumstances subsequent therapy option for patients with ccRCC regardless of their prior immunotherapy status.

Definitions and Measures
Angiomyolipoma: A neoplasm with perivascular epithelioid cell differentiation (PEComa) often associated with tuberous sclerosis. It is characterized by a mixture of epithelioid cells, smooth muscle, vessels, and mature adipose tissue. The kidney is the most common site of involvement. Other sites of involvement include the liver, lung, lymph nodes, and retroperitoneum. The vast majority of cases follow a benign clinical course. However, cases of metastatic angiomyolipomas with sarcomatoid features have been described.

Endometrial Adenocarcinoma: An adenocarcinoma arising from the uterine body cavity. This is the most frequent malignant tumor affecting the uterine body, and is linked to estrogen therapy. Most individuals present with uterine bleeding and are over age 40 at the time of diagnosis. The prognosis depends on the stage of the tumor, the depth of the uterine wall invasion, and the histologic subtype. Endometrioid adenocarcinoma is the most frequently seen morphologic variant of endometrial adenocarcinoma (NCI, 2015).

Karnofsky Performance Status (KPS): A standard way of measuring the ability of individuals with cancer to perform ordinary tasks. The KPS scores range from 0 to 100. A higher score means the person is better able to carry out daily activities. The KPS may be used to determine an individual's prognosis, to measure changes in the ability to function, or to decide if an individual could be included in a clinical trial (NCI, 2015).

Line of Therapy:
- First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
- Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
- Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.

Lymphangioleiomyomatosis: A multifocal neoplasm with perivascular epithelioid cell differentiation (PEComa) affecting almost exclusively females of child-bearing age. It is characterized by the presence of smooth muscle and epithelioid cells and by the

proliferation of lymphatic vessels. Sites of involvement include the lungs, mediastinum, and the retroperitoneum. It usually presents with chylous pleural effusion or ascites (NCI, 2015).

Metastasis: The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.

One line of therapy: Single line of therapy.

PEComa: A soft tissue mesenchymal tumor with perivascular epithelioid cell differentiation (PEComa). Representative examples include angiomyolipoma, clear cell-sugar-tumor of the lung, and lymphangioleiomyomatosis.

Refractory Disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Unresectable: Unable to be removed with surgery.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Torisel (temsirolimus)

Requests for Torisel (temsirolimus) may be approved if the following criteria are met:

I. Individual has a diagnosis of advanced Renal Cell Carcinoma and the following are met (Label, NCCN1, 2A):
   A. Temsirolimus is used as a single agent (monotherapy) in non-clear cell histology RCC for (either 1 or 2):
      1. Relapsed metastatic disease; **OR**
      2. Surgically unresectable stage IV renal carcinoma in individuals with a poor prognosis as manifested by having *at least* three (3) of the following (a through f) (Hudes 2007, NCCN Kidney Cancer Guidelines):
         a. Lactate dehydrogenase greater than 1.5 times the upper limit of normal; **OR**
         b. Hemoglobin less than the lower limit of normal; **OR**
         c. Corrected calcium level greater than 10mg/dL (2.5mmol/liter); **OR**
         d. Interval of less than a year from original diagnosis to the start of systemic therapy; **OR**
         e. Karnofsky performance status 60 to 70 or ECOG performance score of 2, 3, or 4; **OR**
         f. Greater than or equal to 2 sites of metastases;

   OR

   B. Temsirolimus is used for subsequent (second-line) therapy as a single agent (monotherapy) for relapsed metastatic or for surgically unresectable stage IV disease;

OR

II. Individual has a diagnosis of Soft Tissue Sarcoma and the following are met (NCCN 2A):
   A. Temsirolimus is used as a single agent (monotherapy) for sarcoma including, but not limited to, PEComa, recurrent angiomyolipoma, and lymphangioleiomyomatosis; **OR**
   B. Temsirolimus is used in combination with cyclophosphamide and vinorelbine for non-pleomorphic rhabdomyosarcoma;

OR

III. Individual has a diagnosis of Endometrial Adenocarcinoma or Uterine Perivascular Epithelioid Cell neoplasm (PEComa) and the following are met (NCCN 2A):
   A. Temsirolimus is used as a single agent (monotherapy); **AND**
   B. Individual has unresectable, recurrent, or metastatic disease.

Torisel (temsirolimus) may not be approved for the following:

I. Bilirubin greater than 1.5 times the upper limit of normal (ULN); **OR**
II. When the above criteria are not met and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement

policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS	
J9330	Injection, temsirolimus, 1 mg [Torisel]

ICD-10 Diagnosis	
C48.0-C48.8	Malignant neoplasm of retroperitoneum and peritoneum
C49.0-C49.9	Malignant neoplasm of other connective and soft tissue
C54.0-C54.9	Malignant neoplasm of corpus uteri
C55	Malignant neoplasm of uterus, part unspecified
C64.1-C64.9	Malignant neoplasm of kidney, except renal pelvis
C65.1-C65.9	Malignant neoplasm of renal pelvis
~~D30.00-D30.02~~	~~Benign neoplasm of kidney~~
~~D30.10-D30.12~~	~~Benign neoplasm of renal pelvis~~
J84.81	Lymphangioleiomyomatosis
Z85.528	Personal history of other malignant neoplasm of kidney

Document History

Revised: 05/16/2025
Document History:

- 05/16/2025 – Annual Review: No changes. Coding Reviewed: Removed ICD-10-CM D30.00-D30.02, D30.10-D30.12. Added ICD-10-CM C55.
- 05/17/2024 – Annual Review: Clarified existing renal cancer criteria due to NCCN Kidney Cancer guidelines. Add references. Coding Reviewed: Expanded ICD-10-CM coding range C54.0-C54.9. Added C48.0-C48.8 (Effective 05/19/23).
- 05/19/2023 – Annual Review: Update clinical criteria and add for use in Uterine PEComa. Coding Reviewed: No changes.
- 05/20/2022 – Annual Review: Update clinical criteria for use in Rhabdomyosarcoma. Coding Reviewed: No changes.
- 05/21/2021 – Annual Review: No changes. Coding Reviewed: No changes.
- 05/15/2020 – Annual Review: Add labeled contraindications to temsirolimus criteria. Wording and formatting changes. Coding review: No changes
- 05/17/2019 – Annual Review: Initial review of temsirolimus clinical criteria. Minor wording and formatting changes. Coding Reviewed: No changes.

References

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: April 9, 2025.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Hudes GR, Carducci MA, Choueiri TK, et al. Temsirolimus, Interferon Alfa, or both for advanced renal-cell carcinoma. N Engl J Med. 2007; 356:2271-2281.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2025; Updated periodically.
5. NCCN Clinical Practice Guidelines in Oncology™. © 2025 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on April 9, 2025
    a. Kidney Cancer. V3.2025. Revised January 9, 2025.
    b. Soft Tissue Sarcoma. V5.2024. Revised March 10, 2025.
    c. Uterine Neoplasms. V3.2025. Revised March 7,2025.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.