09-J2000-08

Original Effective Date: 3/15/14

Reviewed: 01/08/20

Revised: 02/15/20

Subject: Temsirolimus (Torisel®) Injection

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DESCRIPTION:

Temsirolimus (Torisel®) is an inhibitor of mammalian target of rapamycin (mTOR) and is Food and Drug Administration (FDA)-approved for the treatment of renal cell carcinoma. National Comprehensive Cancer Network (NCCN) Kidney Cancer Guidelines recommend temsirolimus as a first-line option for relapsed or Stage IV disease or as subsequent therapy in patients with predominant clear cell histology. NCCN guidelines also recommend temsirolimus for relapsed or Stage IV disease with non-clear cell histology. Temsirolimus is also recommended by NCCN for certain types of soft tissue sarcoma and uterine carcinomas.

POSITION STATEMENT:

Initiation of temsirolimus (Torisel®) meets the definition of medical necessity when used for an indication in Table 1 and all of the indication specific criteria are met:

Table 1

Indication	Specific Criteria
Kidney cancer	When **ALL** of the following are met: 1. Member is diagnosed with relapsed or stage IV disease 2. Temsirolimus will be used as a single agent

	3. The dose does not exceed 25 mg weekly* 4. **EITHER** of the following a. Temsirolimus is used as first line or subsequent therapy for disease with predominant clear cell histology b. Temsirolimus is used for treatment of disease with non-clear cell histology
Soft-tissue sarcoma (STS)	When used as a single agent and the dose does not exceed 25 mg weekly in members diagnosed with **ONE** of the following: 1. Perivascular epithelioid cell tumor(s) (PEComa) 2. Recurrent angiomyolipoma 3. Lymphangioleiomyomatosis
Uterine cancer (endometrial carcinoma)	When used as a single agent and the dose does not exceed 25 mg weekly for recurrent, metastatic, or high-risk disease
Other FDA-approved or NCCN supported diagnosis (not previously listed above)	When the dose does not exceed the maximum FDA-approved dosing and **ONE** of the following is met: 1. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert) 2. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation

Approval duration: 180 days

Continuation of temsirolimus (Torisel®) **meets the definition of medical necessity** when used as a single agent for the indications in Table 1 and the following criteria are met:

A. The member's disease has not progressed while receiving therapy with temsirolimus

B. The member has been previously approved by Florida Blue or another health plan in the past 2 years, **OR** the member has previously met all indication-specific criteria for coverage

C. The dose does not exceed 25 mg weekly*

Approval duration: 1 year

***NOTE:** Avoid use with strong CYP3A4 inhibitors or inducers. If coadministration of a strong CYP3A4 inducer (e.g., carbamazepine, dexamethasone, phenobarbital, phenytoin, rifabutin, rifampacin, rifampin) cannot be avoided, a dose greater than 25 mg weekly will be permitted for FDA-approved indications. Per FDA-labeling, the dose may need to be increased to 50 mg/week in patients receiving strong

CYP3A4 inducers receiving therapy for renal cell carcinoma. A dose reduction should be considered if coadministration with strong CYP3A4 inhibitors cannot be avoided.

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved: temsirolimus is indicated for the treatment of advanced renal cell carcinoma. The recommended dose is 25 mg infused over 30-60 minutes once a week. Therapy should be continued until disease progression or toxicity. Individuals should receive anti-histamine pre-medication.

Dose Adjustments:

Adverse reactions: interrupt therapy for absolute neutrophil count (ANC) <1000/mm3, platelet count <75,000/mm3, or adverse events of grade 3 or greater according to the Common Terminology Criteria for Adverse Events (CTCAE). Once toxicity has resolved to grade 2 or less, temsirolimus may be restarted with the dose reduced by 5 mg/week to a dose no lower than 15 mg/week.

Hepatic impairment: use caution when treating individuals with mild hepatic impairment. If temsirolimus must be given to an individual with mild hepatic impairment, reduce the dose to 15 mg/week.

Drug interactions: avoid use with strong CYP3A4 inhibitors or inducers. If use cannot be avoided, see prescribing information for dose recommendations.

Drug Availability: temsirolimus is supplied as a 25 mg/mL

PRECAUTIONS:

Contraindications: temsirolimus is contraindicated in persons with a bilirubin greater than 1.5 times the upper limit of normal

Precautions/Warnings

- Hypersensitivity/Infusion Reactions (including some life-threatening and rare fatal reactions) can occur early in the first infusion of temsirolimus; monitor throughout the infusion
- To treat hypersensitivity reactions, stop temsirolimus and treat with an antihistamine. Temsirolimus may be restarted at physician discretion at a slower rate.
- Hepatic Impairment: Use caution when treating individuals with mild hepatic impairment and reduce dose.
- Hyperglycemia and hyperlipemia are likely and may require treatment. Monitor glucose and lipid profiles.
- Infections may result from immunosuppression.

- Monitor for symptoms or radiographic changes of interstitial lung disease (ILD). If ILD is suspected, discontinue temsirolimus and consider use of corticosteroids and/or antibiotics.
- Bowel perforation may occur. Evaluate fever, abdominal pain, bloody stools, and/or acute abdomen promptly.
- Renal failure, sometimes fatal, has occurred. Monitor renal function at baseline and while on temsirolimus
- Due to abnormal wound healing, use temsirolimus with caution in the perioperative period.
- Proteinuria and nephrotic syndrome may occur. Monitor urine protein prior to the start of therapy and periodically thereafter. Discontinue in patients who develop nephrotic syndrome.
- Live vaccinations and close contact with those who received live vaccines should be avoided.
- Women of childbearing potential should be advised of the potential hazard to the fetus and to avoid becoming pregnant.
- Elderly individuals may be more likely to experience certain adverse reactions, including diarrhea, edema and pneumonia.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding:

J9330	Injection, temsirolimus, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity:

C49.0 – C49.9	Malignant neoplasm of 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 unspecified kidney, except renal pelvis
C65.1 – C65.9	Malignant neoplasm of unspecified renal pelvis
D49.2	Neoplasm of unspecified behavior of bone, soft tissue, and skin

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

DEFINITIONS:

None

RELATED GUIDELINES:

Bevacizumab (Avastin) Injection, 09-J0000-66

Pazopanib (Votrient™) Tablets, 09-J1000-49

Sorafenib (Nexavar®) Tablets, 09-J1000-50

Sunitinib (Sutent) Capsules, 09-J1000-51

OTHER:

Table 1: Common Terminology Criteria for Adverse Events v4.0 (CTCAE)

Grade	Description
1	Mild; asymptomatic or mild symptoms; clinical diagnostic observations only; intervention not indicated
2	Moderate; minimal, local or noninvasive intervention indicated; limited age-appropriate instrumental activities of daily living
3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living
4	Life-threatening consequences; urgent intervention indicated
5	Death related to adverse event

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 01/08/20

GUIDELINE UPDATE INFORMATION:

3/15/2014	New Medical Coverage Guideline.
12/15/15	Review and revision to guideline; consisting of updating position statement, description, dosage, coding and references.
12/15/16	Review and revision to guideline; consisting of updating position statement, description, coding and references.
11/15/17	Review and revision to guideline; consisting of updating references.
01/15/19	Review and revision to guideline; consisting of updating position statement, description, precautions, and references.
02/15/20	Review and revision to guideline; consisting of updating position statement and references.