SPECIALTY GUIDELINE MANAGEMENT

AFINITOR (everolimus)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Postmenopausal women with advanced hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer, in combination with exemestane, after failure of treatment with letrozole or anastrozole
2. Adults with progressive neuroendocrine tumors of pancreatic origin (pNETs) that are unresectable, locally advanced or metastatic disease
3. Adults with advanced renal cell carcinoma (RCC) after failure of treatment with sunitinib or sorafenib
4. Adults with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery
5. Adults with progressive, well-differentiated, non-functional neuroendocrine tumors of gastrointestinal or lung origin with unresectable, locally advanced or metastatic disease
6. Adults and pediatric patients with tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected.

B. Compendial Uses
1. Classical Hodgkin lymphoma
2. Osteosarcoma
3. RCC:
   - First-line therapy for relapse or surgically unresectable stage IV RCC with non-clear cell histology
   - Subsequent therapy for relapse or surgically unresectable stage IV RCC with predominant clear cell histology
4. Soft tissue sarcoma subtypes:
   - Perivascular epithelioid cell tumors (PEComa)
   - Recurrent angiomyolipoma
   - Lymphangioleiomyomatosis
5. Thymomas and thymic carcinomas
6. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer
Authorization of 12 months may be granted to members prescribed Afinitor in combination with exemestane for the treatment of HR-positive, HER2-negative recurrent or metastatic breast cancer who meet ANY of the following conditions:
1. The member has been previously treated with tamoxifen.
2. The disease has progressed while on or within 12 months of therapy with a nonsteroidal aromatase inhibitor.

B. Classical Hodgkin Lymphoma
Authorization of 12 months may be granted to members for ANY of the following:
1. Relapsed or refractory classical Hodgkin lymphoma
2. Palliative therapy

C. Gastrointestinal Neuroendocrine Tumors
Authorization of 12 months may be granted to members prescribed Afinitor for the treatment of gastrointestinal neuroendocrine tumors.

D. RCC
Authorization of 12 months may be granted to members prescribed Afinitor for the treatment of relapsed or unresectable RCC and member meets EITHER of the following:
1. For disease that is of non-clear histology, Afinitor will be used as first-line systemic therapy. For disease that is of predominantly clear cell histology, the disease has progressed on prior antiangiogenic therapy (e.g., Avastin, Sutent, Nexavar).

E. Lung Neuroendocrine Tumors
Authorization of 12 months may be granted to members prescribed Afinitor for the treatment of lung neuroendocrine tumors.

F. Osteosarcoma
Authorization of 12 months may be granted to members for the treatment of osteosarcoma.

G. Pancreatic Neuroendocrine Tumors
Authorization of 12 months may be granted to members prescribed Afinitor for the treatment of pancreatic neuroendocrine tumors

H. Renal Angiomyolipoma Associated With Tuberous Sclerosis Complex (TSC)
Authorization of 12 months may be granted to members prescribed Afinitor for the treatment of renal angiomyolipoma associated with TSC.

I. Soft Tissue Sarcoma
Authorization of 12 months may be granted to members for the treatment of any of the following subtypes of soft tissue sarcoma:
1. Perivascular epithelioid cell (PEComa)
2. Angiomyolipoma
3. Lymphangioleiomyomatosis

J. Subependymal Giant Cell Astrocytoma (SEGA) Associated With Tuberous Sclerosis Complex (TSC)
Authorization of 12 months may be granted to members prescribed Afinitor for the treatment of SEGA associated with TSC.

K. Thymomas and Thymic Carcinomas
Authorization of 12 months may be granted to members for the treatment of thymomas and thymic carcinomas.

L. Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma
Authorization of 12 months may be granted to members prescribed Afinitor for the treatment of Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Afinitor [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2016.
2. The NCCN Drugs & Biologics Compendium™ © 2016 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed June 28, 2016. https://www.nccn.org/professionals/drug_compendium/content/contents.asp.
3. The NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 2.2016. Accessed July 28, 2016. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf.
4. Baselga J, Campone M, Piccart M, et al. Everolimus in postmenopausal hormone-receptor–positive advanced breast cancer. *N Engl J Med*. 2012;366(6):520-529.
5. Yardley DA, Noguchi S, Pritchard KI, et al. Everolimus plus exemestane in postmenopausal patients with HR(+) breast cancer: BOLERO-2 final progression-free survival analysis. *Adv Ther* 2013;30:870-884.
6. The NCCN Clinical Practice Guidelines in Oncology: Kidney Cancer. Version 3.2016. Accessed July 28, 2016. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf.
7. The NCCN Clinical Practice Guidelines in Oncology: Hodgkin Lymphoma. Version 3.2016. Accessed July 28, 2016. https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf.
8. Johnston PB, Inwards DJ, Colgan JP, et al. A Phase II trial of the oral mTOR inhibitor everolimus in relapsed Hodgkin lymphoma. *Am J Hematol* 2010;85:320-324.
9. The NCCN Clinical Practice Guidelines in Oncology: Soft Tissue Sarcoma. Version 2.2016. Accessed July 28, 2016. https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf.
10. Sampson JR. Therapeutic targeting of mTOR in tuberous sclerosis. *Biochem Soc Trans*. 2009;37:259-264.
11. The NCCN Clinical Practice Guidelines in Oncology: Thymomas and Thymic Carcinomas. Version 3.2016. Accessed August 1, 2016. https://www.nccn.org/professionals/physician_gls/pdf/thymic.pdf.
12. The NCCN Clinical Practice Guidelines in Oncology: Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma. Version 2.2016. Accessed July 28, 2016. https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf.